NOTE

This Microfiche meets the quality requirements of the American National Standard for Microfiche of Documents (ANSI PH5.9-1975). However, because of imperfections in the document from which it was made, it contains images that are illegible or difficult to read. The source document for this microfiche is the best copy that could be obtained prior to filming.

CIS

Congressional Information Service,
Washington, D.C.

H.R. 4502 AND S. 1966, THE BIOTECHNOLOGY COMPETITIVENESS ACT

HEARING

BEFORE THE

SUBCOMMITTEE ON NATURAL RESOURCES,
AGRICULTURE RESEARCH AND ENVIRONMENT

AND THE

SUBCOMMITTEE ON
SCIENCE, RESEARCH AND TECHNOLOGY

OF THE

COMMITTEE ON
SCIENCE, SPACE, AND TECHNOLOGY
HOUSE OF REPRESENTATIVES

ONE HUNDREDTH CONGRESS

SECOND SESSION

JULY 14, 1988

[No. 138]

Printed for the use of the
Committee on Science, Space, and Technology

H701-28

U.S. GOVERNMENT PRINTING OFFICE
89-952 WASHINGTON : 1988

For sale by the Superintendent of Documents, U.S. Government Printing Office
Washington, DC 20402

COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY

ROBERT A. ROE, New Jersey, *Chairman*

GEORGE E. BROWN, Jr., California
JAMES H. SCHEUER, New York
MARILYN LLOYD, Tennessee
DOUG WALGREN, Pennsylvania
DAN GLICKMAN, Kansas
HAROLD L. VOLKMER, Missouri
BILL NELSON, Florida
RALPH M. HALL, Texas
DAVE McCURDY, Oklahoma
NORMAN Y. MINETA, California
BUDDY MacKAY, Florida
TIM VALENTINE, North Carolina
ROBERT G. TORRICELLI, New Jersey
RICK BOUCHER, Virginia
TERRY L. BRUCE, Illinois
RICHARD H. STALLINGS, Idaho
JAMES A. TRAFICANT, Jr., Ohio
JIM CHAPMAN, Texas
LEE H. HAMILTON, Indiana
HENRY J. NOWAK, New York
CARL C. PERKINS, Kentucky
C. THOMAS McMILLEN, Maryland
DAVID E. PRICE, North Carolina
DAVID R. NAGLE, Iowa
JIMMY HAYES, Louisiana
DAVID E. SKAGGS, Colorado
PAUL E. KANJORSKI, Pennsylvania
GEORGE J. HOCHBRUECKNER, New York

MANUEL LUJAN, Jr., New Mexico*
ROBERT S. WALKER, Pennsylvania
F. JAMES SENSENBRENNER, Jr., Wisconsin
CLAUDINE SCHNEIDER, Rhode Island
SHERWOOD L. BOEHLERT, New York
TOM LEWIS, Florida
DON RITTER, Pennsylvania
SID MORRISON, Washington
RON PACKARD, California
ROBERT C. SMITH, New Hampshire
PAUL B. HENRY, Michigan
HARRIS W. FAWELL, Illinois
D. FRENCH SLAUGHTER, Jr., Virginia
LAMAR SMITH, Texas
ERNEST L. KONNYU, California
JACK BUECHNER, Missouri
JOEL HEFLEY, Colorado
CONSTANCE A. MORELLA, Maryland
CHRISTOPHER SHAYS, Connecticut

HAROLD P. HANSON, *Executive Director*
ROBERT C. KETCHAM, *General Counsel*
CAROLYN C. GREENFELD, *Chief Clerk*
R. THOMAS WEIMER, *Republican Staff Director*

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

JAMES H. SCHEUER, New York, *Chairman*

TIM VALENTINE, North Carolina
DAVE McCURDY, Oklahoma
HENRY J. NOWAK, New York
C. THOMAS McMILLEN, Maryland
GEORGE E. BROWN, Jr., California
GEORGE J. HOCHBRUECKNER, New York

CLAUDINE SCHNEIDER, Rhode Island
ROBERT C. SMITH, New Hampshire
PAUL B. HENRY, Michigan
JOEL HEFLEY, Colorado

SUBCOMMITTEE ON SCIENCE, RESEARCH AND TECHNOLOGY

DOUG WALGREN, Pennsylvania, *Chairman*

BUDDY MacKAY, Florida
LEE H. HAMILTON, Indiana
HENRY J. NOWAK, New York
DAVID E. PRICE, North Carolina
GEORGE E. BROWN, Jr., California
NORMAN Y. MINETA, California
TERRY L. BRUCE, Illinois
CARL C. PERKINS, Kentucky
DAVID R. NAGLE, Iowa
JIMMY HAYES, Louisiana
TIM VALENTINE, North Carolina
JIM CHAPMAN, Texas
DAVID E. SKAGGS, Colorado
PAUL E. KANJORSKI, Pennsylvania
GEORGE J. HOCHBRUECKNER, New York

SHERWOOD L. BOEHLERT, New York
PAUL B. HENRY, Michigan
CLAUDINE SCHNEIDER, Rhode Island
DON RITTER, Pennsylvania
SID MORRISON, Washington
D. FRENCH SLAUGHTER, Jr., Virginia
LAMAR SMITH, Texas
JACK BUECHNER, Missouri
CONSTANCE A. MORELLA, Maryland
CHRISTOPHER SHAYS, Connecticut

---

*Ranking Republican Member.

CONTENTS

WITNESSES

July 14, 1988:

Page

Hon. Robert W. Kastenmeier, a U.S. Representative from the State of Wisconsin 2

Dr. Kathi E. Hanna, Study Director, U.S. Investment in Biotechnology, Office of Technology Assessment 18

Dr. D. Bruce Merrifield, assistant secretary of Commerce for Productivity, Technology, and Innovation, accompanied by deputy assistant secretary Michael Kelley, International Trade Administration 36

Dr. Akihiro Yoshikawa, biotechnology project coordinator, Berkeley Roundtable on the National Economy, University of California, Berkeley 57

Dr. Robert Cook-Deegan, senior analyst, Office of Technology Assessment 77

Dr. Ruth L. Kirschstein, director, Institute of General Medical Sciences, National Institutes of Health 89

Dr. David B. Nelson, executive director, Office of Energy Research, U.S. Department of Energy 149

Dr. Ralph W.F. Hardy, Boyce-Thompson Institute for Plant Sciences, Cornell University, and Biotechnica International, Inc 182

Anne K. Hollander, Conservation Foundation 198

Dr. Bruce F. Mackler, Association of Biotechnology Companies 214

Richard D. Godown, president, Industrial Biotechnology Association 244

H.R. 4502 AND S. 1966, THE BIOTECHNOLOGY COMPETITIVENESS ACT

THURSDAY, JULY 14, 1988

House of Representatives, Committee on Science, Space, and Technology, Subcommittee on Natural Resources, Agriculture Research and Environment, and the Subcommittee on Science, Research and Technology,

Washington, DC.

The subcommittees met, pursuant to notice, in room 2318, Rayburn House Office Building, Hon. James H. Scheuer [Chairman of the Subcommittee on Natural Resources, Agriculture Research and Environment], presiding.

Mr. Scheuer. The Subcommittee on Natural Resources, Agriculture Research and Environment will come to order. This is a joint hearing that we are holding with the Subcommittee on Science, Research and Technology chaired by Congressman Doug Walgren, who will be with us shortly.

Before I make my remarks, I am going to yield to Congresswoman Claudine Schneider, the very distinguished and highly contributing ranking minority member of this committee.

Miss Schneider. Mr. Chairman, I appreciate this opportunity to make my opening statement now.

Regrettably, I must excuse myself to co-chair a hearing in a couple of minutes, but I would like to share with all of you that earlier this week the Congressional Clearinghouse on the Future sponsored a day-long series of panels on emerging issues in biotechnology, including one on agricultural and environmental applications which I moderated. During the course of that day some of the leaders in the field of biotechnology repeatedly pointed to its immense potential, and at the same time they were questioning whether current Federal policy has been designed in such a way to properly direct some of that potential.

I think the need to reexamine Federal biotechnology policy is reinforced by the conclusions of a recent OTA report, also released this week, and one of the main conclusions of the report is that despite substantial public and private investment, current U.S. research may not be sufficient to realize the potential of developments in the field of biotechnology.

Furthermore, lagging could result in the loss of our international edge of this field, which is becoming increasingly crowded with foreign competition. This is an area—and one of few, I regret to say—where the United States does hold a leading edge. Although it is a relatively new industry, it could make a great economic contribution to medicine, to agriculture, and even pollution disposal. Biotechnology products already generate a positive trade balance for the United States, even though our overall manufacturing trade account happens to be in a serious deficit.

OTA points out that in the field of human therapeutics alone, the world market is expected to eventually be worth billions of dollars, while many other countries are pushing forward with their own work. For example, Japan has been conducting research on bacteria that can be used to control pests and viruses that can be used as vaccines against hepatitis and polio, and ways of improving crop productivity.

The three major organizations in Europe also support work in biotechnology, and they are the European Molecular Biology Organization, which is a scientific organization concerned with basic research; the European Economic Community, which has instituted several biotechnology programs; and EURECA, which is a political organization formed to promote collaboration between different countries.

So despite the significant benefits that biotechnology could offer, like many other areas of technology, achieving these benefits presents both promise and peril unless carefully pursued. A thoughtful balance does need to be struck between the careless tinkering with the environment and also the imposition of possibly needless requirements that could prevent the commercialization of extremely valuable products.

I think that today's hearing, given the witnesses that we will be hearing from, will help us to better evaluate whether the current U.S. efforts in this field have been appropriately supported and directed and whether these efforts would be better focused through the creation of some kind of national biotechnology strategy. I would like to commend Chairman Scheuer for his diligence in this area, and I look forward to working with you as well as our other committee members as we consider this issue further.

Thank you, Mr. Chairman.

Mr. SCHEUER. Thank you. Thank you, Congresswoman Schneider.

Congressman Kastenmeier, we are going to be having bells pretty soon, so rather than give my opening remarks now, why don't I call upon you so that if we have to go answer a roll call vote, you won't have to come back here. Would that economize on your time?

Mr. KASTENMEIER. That would be splendid, Mr. Chairman.

Mr. SCHEUER. Then it is a great pleasure for me to call upon one of the most distinguished and thoughtful senior Members of Congress, Congressman Robert Kastenmeier of Wisconsin, who has major jurisdiction and responsibility in the field of biogenetics. It is a pleasure to have you here, Congressman, and we would be delighted to hear from you.

STATEMENT OF HON. ROBERT W. KASTENMEIER, A U.S. REPRESENTATIVE FROM THE STATE OF WISCONSIN

Mr. KASTENMEIER. Thank you, Mr. Chairman. I appreciate the opportunity to participate in your hearings on biotechnology, and I certainly applaud your work and that of the committee in this field.

I have long been a strong supporter of this technology and the industry it has spawned. As chairman of the congressional committee with responsibility for intellectual property protection, in recent years we have succeeded in authoring a number of amendments to protect unique work product of this new science through enhanced intellectual property protection. Even yesterday in the context of the trade bill we passed legislation to enhance process patent protection.

The bills before you today represent an important next step along the road of furthering Government/industry cooperation designed to further the public benefits of biotechnology, and I would like to indicate my general support for H.R. 4502. And, Mr. Chairman, I also support the single change in it that differentiates it from the Senate version, namely in addition to academic and industry representatives, a public interest representative which you would, as I understand, appoint to the board.

The bill pending before your subcommittee which is of the greatest personal interest to me is of course not necessarily H.R. 4502, which you are having hearings on specifically this morning, but rather H.R. 4971, the Transgenic Animal Regulatory Reform Act of 1988. That bill is the product of a series of hearings conducted by my subcommittee over the past year. It is also influenced by the general public debate over the propriety of patenting animals.

As many of you may know, since April of 1987 it has been possible to patent a genetically altered animal—that is, a vertebrate, a mammal—all but human beings themselves. In fact, one such patent was granted to Harvard for a mouse to be used for medical research on breast cancer this April, April of 1988. This development has generated a controversy. Some religious leaders claimed that patenting animals was immoral or perhaps unethical. Farmers expressed concerns about the potential for concentration of economic power in the hands of certain patent holders and, finally—and I know your subcommittee has worked in the area—some environmentalists expressed concerns about the potential havoc of unfettered releasing of genetically altered animals into the environment.

Opposition to the patenting of genetically altered animals produced support for a moratorium on patenting animals. This is embodied in the bill. H.R. 3119, by Mr. Rose. More recently, I offered an alternative to that measure, H.R. 4970, a companion to the bill that I mentioned which is before you, H.R. 4971, that has the net effect of approving the existing state of affairs but creating two exceptions to patent liability for researchers and for farmers. My subcommittee yesterday approved the latter, and by relatively close votes failed to approve a 2-year moratorium which I think, had it been approved, would certainly have sent shock waves through the biotechnology community.

I point that out to sort of bring your committee up to date on what is happening in a companion subcommittee.

One of the concerns about transgenic animals that emerged during the 4 days of hearings that we had, was the adequacy of the existing regulatory framework for biotechnology. Some environmental groups claimed that the existing structure was too informal, without sufficient environmental safeguards. Industry representatives largely felt the framework was more than sufficient Some legal experts also claimed that the regulatory framework, albeit complex and not centralized, was workable.

Without attempting to resolve the merits of that dispute, about which this subcommittee has already heard testimony and received a very important OTA report, there are three regulatory issues that I think merit attention. My own subcommittee deals with the patent issues—but your committee and perhaps two other committees, Agriculture and Commerce, having the regulatory authority—in the bill before you would create a Biotechnology Science Coordinating Committee in a statutory format, which already exists today in the White House by executive order.

Second, as a Member who knows firsthand the existing problems of agriculture, including oversupply even in a drought period, I am concerned as many other Members are with the speed with which the introduction of this new technology will occur within the agricultural community. As a result of this, and in an attempt to forecast what may happen in the future, we have proposed in H.R. 4971 a system of regulation of transgenic farm animals within the Department of Agriculture.

The permit system encompassed in this bill is modeled after a more comprehensive effort offered in the last Congress by our former colleague, Don Fuqua. The bill also creates an Advisory Committee on Transgenic Animals within the Department of Agriculture, and I would expect the advisory committee would include farmers, consumers, scientists, and other knowledgeable and affected parties.

The fourth feature of the bill is a grant of authority to the Environmental Protection Agency to regulate the release of genetically altered animals into the wild. While I recognize in some instances exotic species pose equal or greater danger than genetically altered species, it is still appropriate to flash a warning light with respect to genetically altered wildlife. For example, I have serious concerns, I think one of the early problems might be the release of genetically altered fish into the aquatic environment. I know, for example, in Wisconsin and presumably elsewhere the "super carp" that have been developed genetically, may breed very rapidly and grow to great size, and might indeed be a problem for our lakes and streams in our State and many others.

In sum, Mr. Chairman, I hope my colleagues will look with favor on the concept contained in the bill. I recognize that as introduced it is not ready for enactment, and I have already received a number of valuable suggestions for improving the bill from environmental, agricultural, and business groups. I hope as the legislative process continues, that you will be able to reach in due course a consensus around the regulatory approach suggested by my bill.

I thank you, Mr. Chairman.

[The prepared statement of Mr. Kastenmeier follows:]

STATEMENT
OF
THE HONORABLE ROBERT W. KASTENMEIER
ON
H.R. 4971 - TRANSGENIC ANIMAL REGULATORY REFORM ACT
BEFORE
THE COMMITTEE ON SCIENCE & TECHNOLOGY

Mr. Chairman, thank you for the opportunity to participate in your hearings on biotechnology. I have long been a strong supporter of this technology and the industry it has spawned. As Chairman of the Congressional Committee with the responsibility for intellectual property protection, in recent years I have succeeded in authoring amendments to protect the unique work product of this new science through enhanced intellectual property protection. Most recently we have passed legislation to enhance process patent protection.

The bills before you today represent an important next step along the road of furthering government-industry cooperation designed to further the public benefits of biotechnology.

The bill pending before your Committee that is of greatest personal interest is H.R. 4971, the Transgenic Animal Regulatory Reform Act of 1988. This bill is the product of a series of hearings conducted by my Subcommittee over the past year. It is also influenced by the debate over the propriety of patenting animals.

As many of you may know, since April of last year it has been possible to patent a genetically altered animal. In fact one such patent was granted to Harvard for a mouse to be used for medical research on breast cancer in April of 1988. This legal development generated a tremendous controversy. Some religious leaders claimed that patenting animals was immoral. Farmers expressed concerns about the potential for concentration of economic power in the hands of certain patent holders. Finally, some environmentalists expressed concerns about the potential havoc of unfettered releasing genetically altered animals into the environment.

Opposition to patenting animals produced support for a moratorium on patenting animals. This proposal is embodied in H.R. 3119, by Mr. Rose. More recently, I offered an alternative to that measure, H.R. 4970, that has the net effect of approving of the existing state of affairs, but to create two exceptions to patent liability -- for researchers and farmers. My Subcommittee is scheduled to mark-up these two bills on July 13, 1988.

One of the concerns about transgenic animals that emerged during the four days of hearings we held on this issue was the adequacy of the existing regulatory framework for biotechnology. Some environmental groups claimed that the existing structure was too informal, and without sufficient environmental safeguards. Industry representatives asserted that the existing regulatory framework was more than sufficient. Several legal experts also claimed that the regulatory framework -- albeit complex -- was workable. Without attempting to resolve the merits of that dispute -- about which this Subcommittee has already heard testimony and recently received an important OTA study -- there are three regulatory issues that I believe merit attention.

First, the Congress should create the Biotechnology Science Coordinating Committee in a statutory format. In my opinion the linchpin to the current loose regulatory "confederation" between the various agencies is the BSCC. It would be a mistake to permit the Executive branch to disband the BSCC without Congressional approval.

Second, it is important to recognize the nature of the work being done on transgenic animals including that by the Federal government. The National Institute of Health is already spending well in excess of $16 million on developing transgenic animal research, primarily aimed at biomedical research. This type of research is already well regulated by the existing NIH guidelines.

In addition, the United States Department of Agriculture is devoting substantial resources to developing transgenic farm animals. Unfortunately, I have less confidence in their ability to regulate this work or similar work undertaken by private parties without USDA funds.

As a result of the work on transgenic animals for agricultural purposes scientists hope to produce more efficient meat and dairy production, disease resistant animals and leaner food products. As a Member who knows first hand the existing oversupply of many agricultural products, I am concerned about the speed with which introduction of this new technology will occur within the agricultural community. As a result of this concern I have proposed in H.R. 4971, a system of regulation of transgenic farm animals within the Department of Agriculture.

The permit system encompassed in this bill is modelled after a more comprehensive effort offered last Congress by our former Colleague Don Fuqua. I expect that initially the USDA will be required to issue permits for all classes of experiments in this area of research regardless of the source of the funds. Once an experiment has succeeded, further USDA approval would be required to permit expanded experimentation or, subsequently, full scale commercialization. The criteria to be applied by the USDA would be a requirement that the researcher prove that the work does not pose an unwarranted risk to human health, welfare or the environment. Also, because I expect that the learning curve will become more advanced, the USDA is given statutory authority to waive the permit requirement for classes of experiments that are presumptively safe.

The bill also creates an Advisory Committee on Transgenic animals within the Agriculture Department. I would expect this Advisory Committee will include farmers, consumers, scientists and other knowledgeable and affected parties.

The third important feature of the bill is the grant of authority to the Environmental Protection Agency to regulate the release of genetically altered animals into the wild. While I recognize that in some instances exotic species pose equal or greater danger than the genetically altered species. It still seemed appropriate to flash an amber light with respect to genetically altered wildlife. I have serious concerns about the release of genetically altered fish into the aquatic environment. This section of the bill does not spell out the exact nature of the regulatory mechanisms to be used, in order to permit this Committee to make those judgments after the hearing process has run its course.

In sum, I hope that my colleagues will look with favor on the concept contained in this bill. I recognize that as introduced, this bill is not ready for enactment. I have already received a number of valuable suggestions for improving the bill from environmental concerns, agricultural groups and business groups. I hope that as the legislative process continues that you will be able to reach a consensus around the regulatory approach suggested by this bill.

Mr. **Scheuer**. Thank you very much, Congressman.

You have jurisdiction over the Patent Office in your committee.

Mr. **Kastenmeier**. Yes, we have jurisdiction over the Patent Office, and I might parenthetically say, Mr. Chairman, you will see in your OTA report something we have been aware of recently, that the grants of patents for biotechnology have been slowed down. We have a hearing scheduled; we had one scheduled which we had to call off because we were preempted by the drug bill being in the full committee. You will note that we——

Mr. **Scheuer**. You have a hearing scheduled on this subject, on the backlog?

Mr. **Kastenmeier**. On the question of backlog of patent applications within the Patent Office. We consider that a very serious problem. We know that the community, many of the community represented in your panels here this morning. are aware of that, and we hope to confront the Patent Office and make some suggestions for meeting that problem.

Mr. **Scheuer**. Very good. As I understand it, they have 7,000 applications pending and they take approximately 2 years before they even open the covers of an application and begin to look at it. Meanwhile we are in this race against time, competing desperately with other countries that have got their institutional act together and that are moving very swiftly to overtake us.

We know they can do it when they put their minds to it. When the Japanese decided that they were going to target computer chips, they did it, and they wiped us out in that field. When they decided that they were going to target robotics, they did it, and they totally eliminated us in global commerce in that field, also. So for our Patent Office to be fiddling while Rome burns and to waste several years before they even begin to look at an application seems absolutely aberrational and totally harmful, and I couldn't be more pleased that you are taking it up.

Congressman Paul Henry?

Mr. **Henry**. Thank you, Mr. Chairman. I note that on the Smithsonian, the Mall, this week we are celebrating, I believe, the 60th birthday of Mickey Mouse, and I don't know how old Mighty Mouse is, and our distinguished colleague has told of the introduction of Harvard mouse. There is a lot of fear——

Mr. **Scheuer**. Is this part of the Harvard boutique conspiracy?

Mr. **Henry**. The Harvard boutique? No, I was not trying to make that connection.

I do want to deal with one thing that really genuinely does concern me, the danger of overreaction, of ethical fears in biotechnology. The analogy is terrible because we are talking about different kinds of mice, but 60 years ago ethicists were very upset, many of them, over Mickey Mouse because they opposed the cinema. Mighty Mouse created problems because it induced violence, and there are all kinds of concerns, some legitimate, I presume, but also I imagine some that time will prove not to be legitimate, on Harvard mouse—the little mouse, not the big one. I had better be careful. You started that, Mr. Chairman. [Laughter.]

Mr. **Scheuer**. Is this going to develop into a vicious partisan——

Mr. **Henry**. I never thought we would do that here, not in this committee.

I think there is a very real fear that the policy board and its advisory panels have not only the potential to enhance biotechnological development but in a sense to become a sounding board that puts unreasonable brakes on biotechnology breakthroughs. I wonder if you would like to respond to that, because I know you have heard that charge and it is one which I think is going to concern this panel somewhat.

Mr. **Kastenmeier**. Well, of course that fear exists, even as the other fears exist, that is to say what the research, what the development, the patenting, the commercialization in the area of biotechnology or in genetically altered animals will produce. Obviously I think we should seek a balance. We would not want to impede research, development, and ultimately commercialization of these products. As the Supreme Court said, you can no more do that than Canute could hold back the tides. This is coming and we will have to deal with it.

The ethical problems are extremely complex. I know personally I wrestled with that for a long time and decided that at least not in any of my bills could I address that, that is to say, to suggest statutory standards. So I think we will have to depend, I suspect, on bioethical committees with a makeup which would be reliable in terms of considering these—I say reliable in a sense of not holding back that which I think the national community would want to see developed and available, and on the other hand prevent the horror stories that some people think are still possible.

I think we can largely be assured by the NIH guidelines affecting genetically altered animal research in the past 15 years. We have not seen the sort of horror stories that one would expect in terms of what is produced by that system. Therefore, I think we have something very positive to build on, and I do not think that to date we have seen an inhibition in research and development. I think that any committees or commissions or forums that we create for consideration of biomedical ethics or other ethical problems, if balanced, can produce the kind of result we want.

But I do think that there are enough people who are concerned in the country that we ought to have some sort of overview, if not by the Congress itself, obviously by some sort of authority, a forum that has the sort of integrity that the national community will recognize. It may be that they will attempt, that there are some forms of research or some possible developments that they would recommend against, but I think we are in pretty good hands.

I think it has reached the point, however, that the bill basically that you have before you this morning and the other piece on the bioethical question in the Commerce Committee need to come together. I think we do need a statutory response. We have been aware of this for at least 15 years, and decided to turn it over to the scientists in NIH for that period of time, so I trust the time has come for us to respond legislatively but not to overreact. I think the gentleman's question is a good one, is the central one in the process.

Mr. **Henry**. I don't want to presume on the time because I know we have other Members here and we are all fearful of that first vote.

Mr. **Scheuer**. Surely.

Mr. **Henry**. In most of the major areas of science that this committee explores, we over and over again run into the pattern where we are at the top of the heap in terms of fundamental research and lagging in applied research. In this area, for a number of reasons, we find ourselves well ahead in applied research and bemoaning the lack of fundamental research.

It seems to me a kind of inconsistency in terms of our approach to the dilemma, or some of the dangers in terms of allowing Government to try in some respects overly—the problem is always overly—to get involved in these allocative questions. For example, in the OTA report we are told that while there is a lot of fundamental research in the medical biotechnology because the commercial spinoffs in the market are immediately foreseeable and overwhelming, that tends then to distort and bring the fundamental research away from agricultural or waste management types of research.

I just have to make this observation, how ironic it is, because normally we are here—for example, in our National Science Foundation markups for several years, most of the people on this committee and the SRT Subcommittee have bewailed the fact that we are so basic research oriented, we haven't done enough to prompt applied research. Now we are coming to this and saying how do we get the basic research there so we don't lose our markets, lest someone else come in with government-supported basic research. We are doing just the opposite. I wonder if you might give us some guidance on that issue?

Mr. **Kastenmeier**. I find that I can't really—I don't differ with the basic analysis that you have made. I think throughout, however, the Congress has seen this—I know my own institution at the University of Wisconsin sees this as a cooperative effort and is increasingly interested in industry applications of its basic research, and I think this is generally the case. I agree that this is an area where we are basically ahead in the world, although Japan and other countries have the capability of catching up quite quickly, and so we do have a responsibility, I think, not to smother our research through overreaction or smother our application and commercialization of our research.

I don't know whether we are behind in basic research. As you point out, the biomedical field is more productive, and I don't think you can hold back the biomedical field in any event. It is going forward, we notice in the patent areas that that was the first patent issued, and it is probable that many early patents will relate to biomedical transgenic animals rather than to farm animals or other animals.

But I guess I would generally agree with the gentleman's comments. I think that it is hard for me to judge whether or not we have been, as the Federal Government, sufficiently patrons of basic research in the area, or have inhibited private research in the area, let's say in the last 10 or 15 years. It is difficult for me to make that assessment, but I do think the outgrowth of literally thousands of small companies that deal in, that develop and use biotechnology, suggests to me that we are going ahead satisfactorily with respect to the application of our research.

Mr. HENRY. Just to follow up the last question, if I may, maybe I might venture the unthinkable. Maybe this area has blossomed so beautifully in our country because the Government has stayed out of getting involved in directed, centralized research and you have had this tremendous blossoming of small, entrepreneurial research activity, much as in the software market in computers, for example, where many flowers have indeed bloomed and it has turned out to be much better than going through the established research centers and the giants that would have the ability to work, to be part of a centralized planning council that the Government would put together.

I am not trying to bait you but I am trying to be a devil's advocate on this thing. Why is it that it has gone so well, if Government has in fact been characterized by such benign neglect in this area as it has, whereas in other areas of science where we are heavily involved in fundamental research, the applications technology is lacking?

Mr. KASTENMEIER. That appears to be the case, and probably we have developed our Government-sponsored research in other areas than biotechnology, obviously military and other applications, which I don't know is necessarily altogether all that good, but nonetheless that is the case. But I think this has been an area which has been fruitful in terms of commercialization, application, and in which we find clusters of small companies around research centers, university research centers. The bill itself reflects this in terms of the academic and the industry partnership, in terms of who will make the policy decisions here, and I think it has worked very well.

I don't know whether, other than biotechnology, whether the same analogy would hold or not, that is to say, whether you could have decentralized research in certain other fields and it would be as effective and profitable as it was, as it apparently has been in the biotechnology field. Possibly. I really don't know, but I think the basic conclusion the gentleman has reached, namely that the minimal contribution by the Federal Government to date to this area has obviously not hindered its development, is the case. But again I would suggest this does not mean, however, that at this point in time there is not a role for appropriate either regulatory or other type of legislation in the area, but that has to be a balanced approach and we obviously should not kill the baby in the bath, so to speak.

Mr. SCHEUER. Just a footnote to your remarks, Congressman. You say we are doing so well. You asked me before the hearing started, how was my wife, and I said, "Compared to whom?" Well, I would say the same thing when you say we are doing so well: Compared to whom? Compared to the Japanese or the West Germans? If you look at the accelerating rate of their progress since they have started seriously in the field of biotechnology, and just extrapolate that curve, I think you would find that if we don't do something very radical they are going to pass us.

Now the total amount that Government is investing, of about $2.7 billion, is far in excess of what private industry is investing. They are investing far less than that, the total of all of them, the 400 small firms and the 70 or so larger firms. While there is a lot going on in the field of biotechnology, there is far less going on in the field of agriculture, animal research; very much less going on in environmental research, in areas like toxic wastes, oil spills, and the like.

So if you compare our progress either to the need or what other countries have done during this decade, I think you will feel that the order of magnitude of what is happening in this country is far less than it could be and far less than it should be, but we will get into that in the course of this hearing. That's what the hearing is all about.

Congressman, we appreciate your testimony very much. You did refer to the Harvard mouse. Can you give us some examples for the record, so that people can understand, what we are talking about when we talk about genetically altered animals? What do they look like? What are they like? What is the purpose for which we are engaging in the genetic alteration of animals?

Mr. **Kastenmeier**. Well, I don't claim to be an expert in this but obviously we are talking about animals in which a gene sequence has been implanted which will produce certain desired characteristics in the animal—in agriculture, disease resistant animals, leaner animals, et cetera. The Department of Agriculture itself has conducted a number of these experiments that are said to be capable of reproduction. The benefit over normal breeding techniques is, this can be achieved in a time frame that is useful within months and years rather than in generations.

The medical research, of course, will cause the mice or other types of experimental animals to develop traits in which certain illnesses or certain diseases can be differentially tested, as we could not effectively do with human beings, and that is precisely what occurred with Dr. Leder's mouse. That seems to be the primary purpose of the application of genetic alteration of animals up to this point in time. We are familiar with the earlier *Chakrabarty* case in terms of microorganisms being used to eat oil spills. You are well aware of that, but the mammals and vertebrates are used principally for two purposes as we see it: for biomedical research and for developing farm animals in a shorter period of time, with enhanced characteristics with respect to production and value in terms of a farm commodity.

Mr. **Scheuer**. Anything else, Paul?

Mr. **Henry**. No.

Mr. **Scheuer**. Well, thank you very much, Congressman Kastenmeier. Your testimony has been very helpful. We are grateful to you for appearing here this morning.

Mr. **Kastenmeier**. Thank you, Mr. Chairman.

Mr. **Scheuer**. I think the testimony of Congressman Kastenmeier and the discussion that it engendered gives us some feeling of the extraordinary importance that we all attach to this issue of biotechnology and its enormous potential impact on not only our well-being through biotechnology advances in health and in animal husbandry and controlling the environment, but also the economic benefits to our country of this trade that we estimate will be $40 billion annually by the end of the century, and which the Japanese estimate will be closer to $100 billion by the end of the century. So I am sure Congress will be more and more involved in every aspect of the regulation, encouragement and focusing of national concern on biotechnology.

In prior hearings this committee has considered whether the Federal regulatory structure was adequate to deal with biotechnology and its products. It has been 4 years since the administration first proposed guidelines for the coordinated Federal regulation of biotechnology. Many of these guidelines have not yet gone into effect, and this has provided a certain amount of regulatory uncertainty.

In the meantime, as we mentioned before, more than 7,000 applications for biotechnology patents are piled up in the Patent Office and languishing there for lack of attention, each one enjoying a 2-year wait before the covers of the application are even opened by the patent people, while as I say, abroad our competitors in global commerce have targeted biotechnology as a top priority and are racing ahead in its development. For us to be involved in this global race against time to assure our eminence in biotechnology, while one particular Government agency provides this absolutely inexplicable bottleneck, is hard for any rational person to understand. Abroad, foreign countries and foreign corporations simply steal our biotechnology products, and they do that with impunity because of flaws in our patent protection system.

Despite this daunting obstacle course, the U.S. biotechnology industry is very busy conducting research and testing and bringing important new products to the market. This leads me to mention Dr. Samuel Johnson's famous quote where he says, "The important thing about a dog dancing on its hind legs is not that it is well-done but that it is done at all." It is remarkable that our biotechnology industry has made as much progress as it has, with government regulation that is full of gaps and flaws and lassitude, indifference, time-wasting and overregulation.

It is amazing that the industry has made as much progress as it has, and it is high time for Congress to get its institutional act together and stop the overregulating where that is taking place, to commence regulating where there is an absence of adequate regulating, and to target opportunities for biotechnology products where the economic incentives may not be sufficient to the magnitude of the job, and the pace with which our national interest dictates that we move ahead in these important fields.

It is quite true that the United States has carved out initial preeminence in the field of biotechnology, but it is by no means true that this is going to continue without a vast acceleration of our efforts. I mentioned before what happened when the Japanese decided to target computer chips, to target robotics, and to focus the attention of their scientists and their financial mechanisms to these fields of top priority concern to them. The fact is, they wiped us out in both of these fields. We are choking on their exhaust gases, and I don't think any of us want that to happen in the field of biotechnology. That is a major purpose—not the only purpose but certainly a major purpose—of this hearing and this committee's concern.

We all know that Japan has targeted biotechnology as a key area of development interest, and they have launched a joint government/industry effort to dominate this global marketplace by the turn of the century. We all wish them luck. There is no question that their efforts, as well as our efforts collectively, will benefit mankind. We look forward to the work of their efforts, but we have no intention of abandoning the global marketplace to them, as we were forced to do in these other fields that I have mentioned. We must respond, if we are going to avoid that, with our own national strategy for biotechnology.

The bills we are considering today, H.R. 4502, which is coming out of this committee. Its companion bill, S. 1966, was introduced by Senator Lawton Childs, who has been a major force and a very constructive one in the field of biotechnology. These two bills would establish a national commission to examine the entire range of cross-cutting issues that affect the commercialization of biotechnology. The commission would report to the President and the Congress on policies to enhance the competitiveness of U.S. industry and maintain our scientific leadership in the field of biotechnology.

The Senator's bill would also establish a panel to guide the Government's efforts to map the human genome, a major scientific initiative with enormous implications for biotechnology. Now the Office of Technology Assessment has provided the committee with a thorough analysis, an excellent analysis, of the present biotechnology efforts in its report, "U.S. Investment in Biotechnology," and Kathi Hanna will testify in the next few minutes in summing up that committee's report. Her brilliant, marvelous testimony itself could be a guide for this country to act in the next few years, but we will all get a very clear idea in summary form of the work of that commission from Kathi Hanna's outstanding, excellent testimony.

She observes that despite considerable Federal support for biotechnology R&D, there are several very important areas which are underfunded. Amongst them are agricultural research, especially in the field of crop genetics, and research into the use of genetically engineered organisms to clean up hazardous waste, oil spills, and the like. These are critical areas which require further Government support, significant Government support, perhaps because the free enterprise community hasn't divined the profit lure hanging out there that would drive their research efforts and the financial support that that would require.

Now today the subcommittee will hear from a very distinguished group of witnesses with a variety of backgrounds and viewpoints on biotechnology, and we are looking forward to their advice and counsel on what we have to do to maintain our lead in the biotechnology industry and our biotechnology competitiveness in the global marketplace. Also we look forward to their advice on how we make progress in moving ahead and divining and unraveling the mysteries of the human genome.

Paul?

Mr. **Henry**. I have no opening statement, Mr. Chairman.

Mr. **Scheuer**. Now I am happy to recognize our colleague, Tom McMillen, from the State of Maryland.

Mr. **McMillen**. Mr. Chairman, thank you very much, and I would ask unanimous consent that my written statement be included in the record. I would like to commend you for holding these hearings and your leadership on this whole issue of trying to establish a national strategy, a national biotechnology commission to direct our efforts in this regard.

When I was reading the New York Times article the other day, I couldn't help but notice the comment that biotechnology will be the core technology for the next industrial revolution, and I think that is——

Mr. SCHEUER. For the postindustrial revolution.

Mr. MCMILLEN. For the post or the next industrial revolution, postindustrial revolution, whatever. I think it is very, very important that we explore these issues in great depth, not only the quantities of monies that the Federal Government is spending in this area but the quality of monies as well; a point that you just mentioned, are we spending enough in the environmental and agricultural areas? You know, how do we maintain our lead in these areas, to prevent the United States from becoming complacent and lethargic in the years ahead? To me this is a key industry for the future of this country. It is a key industry for the future of Maryland, it is a key industry for the future of North Carolina, and I am particularly pleased that you are moving ahead on these issues, Mr. Chairman. Thank you.

Mr. SCHEUER. Now I would like to recognize Congressman David Price. I want to point out when I recognize him that North Carolina is spending almost $7 million, the State of North Carolina is spending almost $7 million in support of biotechnology efforts in that State, and that state is second only to New York. It is the number two State in the Nation encouraging biotechnology, and I commend the gentleman. If he has any explanation for this really remarkable performance by his State, I hope he will include that in his remarks.

Mr. PRICE. Well, thank you, Mr. Chairman. I don't have a prepared statement. I do want to commend you for holding these hearings and look forward to hearing from our witnesses.

You are absolutely right, that my State of North Carolina has seen the future and has chosen to invest in a major way in biotechnology. We have underway what I believe is a landmark cooperative effort between our universities and State government and the private sector, and the Biotechnology Center of North Carolina stands as a monument to that.

I look forward very much to these hearings and to the kind of information that is going to be developed here this morning.

Mr. SCHEUER. Thank you much, Congressman.

Okay. The first panel will be on the question of U.S. competitiveness compared to other countries and how we would propose to maintain our lead, maintain our current position of leadership: Dr. Kathi Hanna, whom I referred to before, who is project coordinator of this assessment of biotechnology; Dr. Bruce Merrifield, Assistant Secretary for Productivity, Technology, and Innovation of the Department of Commerce; and Dr. Akihiro Yoshikawa, the biotechnology project coordinator at the University of California Berkeley and a member of the Berkeley Roundtable on the International Economy. Would all of you come to the witness table, if you would?

Dr. Yuan, is this the panel that you would like to accompany? Would you like to come up and sit with Dr. Merrifield?

Dr. YUAN. I will let Mr. Kelley do that.

Mr. SCHEUER. Pardon me?

Dr. YUAN. I will let Mr. Kelley do that.

Mr. SCHEUER. All right. Well, Kathi Hanna, why don't you take us to the mountaintop and give us your views? As I say, your testimony was absolutely brilliant and we really benefitted from it. Why don't you take, each of you, 7 or 8 minutes, and then I am sure we will have some questions for you. If you can, try not to read your testimony. We have read it all. Just chat with us as if we were in a living room together. Okay?

Dr. Kathi Hanna.

STATEMENT OF DR. KATHI HANNA, STUDY DIRECTOR, U.S. INVESTMENT IN BIOTECHNOLOGY, OFFICE OF TECHNOLOGY ASSESSMENT

Dr. HANNA. Thank you, Mr. Chairman.

I am Dr. Kathi Hanna of the Office of Technology Assessment, and I was study director of the OTA's special report, "U.S. Investment in Biotechnology" which was released by your subcommittee on July 12th. This morning I will give a brief overview of the OTA report and describe its principal findings.

As you mentioned earlier, OTA found that 12 Federal agencies and one cross-agency program spent roughly $2.7 billion on biotechnology R&D in fiscal year 1987. The National Institutes of Health contributes by far the largest share of that support at $2.3 billion or roughly 84 percent. Significant investment is also being made by the Department of Defense, the National Science Foundation, the Department of Energy, and the Department of Agriculture, and I refer you to Table 1 in my written testimony for those exact figures.

In addition to investment by the Federal Government, some 33 States are actively engaged in some form of promotion of biotechnology. These efforts are seen as a means to achieve academic excellence in their State colleges and universities, as a means of economic development, or both. State investment totaled $147 million in fiscal year 1987, with three States making up more than half of that investment, and I refer you to Table 2 of my written testimony.

Mr. SCHEUER. Just tell us which three States. New York, New Jersey, and North Carolina?

Dr. HANNA. New York, Pennsylvania, and New Jersey. North Carolina comes closely after that.

Mr. SCHEUER. I see.

Dr. HANNA. In the private sector, OTA found commercialization of biotechnology by U.S. industry to be healthy and competitive. As mentioned earlier, OTA identified 403 American companies dedicated to biotechnology and an additional 70 established corporations with significant investments. Combined, U.S. industry is spending an estimated $1.5 to $2 billion on biotechnology R&D.

Because biotechnology has become an essential tool for many industries, there is no such entity as "the biotechnology industry." Rather, biotechnology is a set of tools employed by several industrial sectors, each with its own advantages and obstacles in the race to market. Human health care, primarily therapeutics and diagnostics, continues to be the focus of most R&D investments, with chemicals ranking second and agriculture third as fields of application, and I refer you to Table 3 in the written testimony.

The boom time for the formation of biotechnology companies was in the period 1980 to 1984. Consolidation within the industry and the predominance of a few firms has slowed that growth formation. Nevertheless, the amount of money invested by large, more diversified firms continues to grow. OTA found that strategic alliances between large corporations and smaller dedicated biotech companies are increasing, and are seen as a means of financial strength. Instability in the financial markets may accentuate the dependence of many smaller companies on the larger established corporations.

OTA found that industrial alliances occur between U.S. companies rather than between U.S. and foreign companies at a greater rate. The most common form of U.S.-foreign collaboration, when it does occur, is with Japanese firms, overwhelmingly in the field of human health care.

To date, dedicated biotechnology companies have raised over $5 billion from private investors, yet 80 percent of that investment has been made in 10 companies. Investment in health care applications accounts for 75 percent of total private investment. Agricultural applications have received only 16 percent of total private investment.

To illustrate the diversity of issues facing commercial biotechnology, OTA examined three industrial applications—human therapeutics, plant agriculture, and hazardous waste management. In human therapeutics, biotechnology represents an area where there has been substantial Federal support. As a result, the knowledge base is vast and growing, the commercial aspects enticing, and the regulatory regime similar to that applied to more traditional approaches of drug design and manufacturing.

In contrast, plant biotechnology faces a much smaller knowledge base, due to lower levels of Federal support for basic research in the plant sciences. Despite the great promise in this area, success is by no means assured. Of all the problems facing agricultural research, the most pressing is the need for increased Federal support.

The application of biotechnology to waste disposal is still largely experimental and the investment is small compared with that in other areas, but biotechnology's potential to remedy waste problems remains undeveloped due to a variety of technical, institutional, economic, and perceptual barriers. The EPA is the lead agency in conducting research and development in waste disposal, but there is a near consensus among scientists and industrial managers that EPA does not give appropriate weight to biotechnological approaches.

In terms of overall employment in biotechnology, the number of jobs has grown over the past decade. OTA found that in 1987 there were nearly 36,000 jobs in the field, of which almost half are for scientists and engineers. Despite growth in employment in recent years, however, biotechnology is not expected to become a major industrial employer as compared to other sectors.

The NIH, by far the largest source of fellowships and training grants, is also the largest supporter of such training for biotechnology, yet the share of NIH's research budget devoted to training has shrunk from a high of 18 percent in 1971 to a low of less than 4 percent in 1987.

That concludes my summary of the principal findings. The report identifies 10 policy issues related to this topic that today confront Congress. I will very briefly discuss several of these policy issues.

An issue central to the findings of the report pertains to the adequacy of Federal support for R&D relevant to biotechnology. There are no objective and reliable measures for determining whether current Federal support for biotech R&D is sufficient. Clearly, intensive and sustained Federal support in applications of biotechnology to the life sciences has been transformed into commercial products, in some industries much faster than in others.

The slow pace of progress in the less developed applications of biotechnology is often due to insufficient funds for basic research, while in other cases potential products are simply not being developed because industry does not consider the biotechnology product or process sufficiently better than conventional methods. Furthermore, excessive regulatory burdens or public perceptions associated with applications of recombinant DNA can be more important factors than underfunding in some biotechnology applications.

Anecdotal evidence suggests that the current system of research support in the United States sometimes fails to fill critical gaps between basic research and development. Gaps could be filled through additional financial support for applied research, technology transfer, and increased Federal support for multidisciplinary programs.

An issue raised in the OTA report concerns the need for more interagency cooperation in funding biotechnology R&D. Congress could establish an interagency coordinating body to identify areas of research that could be co-funded across agencies, address solutions to filling research needs, and develop strategies to promote tech transfer.

Under the Federal Technology Transfer Act, directors of Government-operated Federal laboratories may enter into collaborative R&D agreements with other Federal agencies, State and local governments, industrial organizations, and nonprofit organizations. OTA found that biotechnology is an area of research currently pursued by many Federal laboratories that could be more effectively shared with industry and universities through active compliance with that act.

OTA identified several issues pertaining to the effect of the Tax Reform Act of 1986 on firms commercializing biotechnology. Current provisions include extension and reduction from 25 to 20 percent of the R&D tax credit, repeal of the investment tax credit for equipment investment, and abolition of the preferential treatment for capital gains. These provisions are expected to have a negative impact on the ability of small biotechnology companies to obtain funds for R&D.

An additional issue addressed in the report focuses on growing concern that U.S. trade policy toward high technology goods that could compromise national security poses a potential threat to the growth of biotechnology exports. A technical advisory committee within the Department of Commerce was formed in 1985 to address this issue, but the committee efforts to date have been marginal.

As more and more biotechnology products become available for export, there is some concern on the part of industry that these products will become caught between the interests of Commerce and Defense or will become delayed due to administrative confusion about the required approval process.

Finally, OTA reports that patent litigation in biotechnology is likely to increase, given the complex web of partially overlapping patent claims. How the courts uphold patents and interpret new ones, as well as how well U.S. companies are able to protect U.S. patents abroad, will be issues facing the biotechnology front-runners in the next few years. In addition, as mentioned earlier, there are nearly 7,000 biotechnology patents pending at the U.S. Patent and Trademark Office.

In summary, several conclusions are apparent about the nature of U.S. investment in biotechnology. First, the level of investment is insufficient to meet the promise suggested by current work in many areas. Second, biotechnology is a set of tools used in many industrial sectors. Each area of application presents a different set of issues for debate due to differences in the state of the art, levels and proportions of public and private support, the effects of regulation, and the degree of commercialization. As Congress discusses the various options by which to safely promote the growth of these industries, the diversity of issues facing these many sectors must be recognized.

Thank you, Mr. Chairman.

[The prepared statement of Dr. Hanna follows:]

TESTIMONY OF KATHI E. HANNA
OFFICE OF TECHNOLOGY ASSESSMENT
U.S. CONGRESS

BEFORE THE
SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURAL RESEARCH
AND ENVIRONMENT
HOUSE COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY

July 14, 1988

U.S. INVESTMENT IN BIOTECHNOLOGY

Thank you, Mr. Chairman. I am Kathi Hanna of the Office of Technology Assessment (OTA), study director of the OTA special report *U.S. Investment in Biotechnology*, published July 12, 1988.

This morning, I will give a brief overview of the OTA report and describe its principal findings.

Summary of Findings of the OTA Report

Since the discovery of recombinant DNA in the early 1970s, biotechnology has become an essential tool for many industries. The potential of biotechnology to improve the Nation's health, food supply, and the quality of the environment leads to questions of whether current levels of investment in research and development, human resources, and policy formulation are adequate to meet these expectations.

Any analysis of spending in biotechnology is confounded by wide variation in the definitions used by various sectors to describe biotechnology, and in the methods used to account for that investment. As a consequence, figures on expenditures are approximate and the scope of investment cannot be precisely determined. It is important to look beyond the numbers to the enormity and diversity of efforts underway within the United

States to support research in biotechnology and its various applications. For the purpose of the OTA report, however, biotechnology, broadly defined, includes any technique that uses living organisms (or parts of organisms) to make or modify products, to improve plants or animals, or to develop micro-organisms for specific use. The report focuses on "new biotechnology" (e.g., recombinant DNA techniques, cell fusion, and novel bioprocessing techniques) rather than "old biotechnology" (e.g., use of micro-organisms for brewing and baking or selective breeding in agriculture and animal husbandry).

OTA found that twelve Federal agencies and one cross agency program spent roughly **$2.7 billion in fiscal year 1987** in support of research and development in biotechnology-related areas. The National Institutes of Health (NIH) contributes by far the largest share of that support, approximately $2.3 billion or 84 percent. Significant investment is also being made by the Department of Defense, $118.8 million; the National Science Foundation, $93.8 million; and the Department of Energy, $61.4 million. The Department of Agriculture expects to fund some $84 million in biotechnology research, divided between the Cooperative State Research Service and the Agricultural Research Service (see table 1).

In addition to investment by the Federal Government, some 33 States are actively engaged in some form of promotion of biotechnology research and development. These efforts are seen as a means to achieve academic excellence in their colleges and universities or as a path to economic development, or both. State investment totaled $147 million in fiscal year 1987, with three States making up more than half of that investment (see Table 2).

States have differing expectations about their return on biotechnology investments. Some spend money to strengthen university faculties so that private business development is aided and encouraged. Others offer direct incentives to industry, including facilities and tax advantages. Regardless of their approach, successful programs rely on a strong academic and research base, venture capital, and an unusually vigorous interaction among researchers, manufacturers, users, and State officials.

With the oldest State program (North Carolina) only in its seventh year, it is too early to judge the success of State efforts. The only available measures of success are indirect ones, namely, the size of the budget, the number of biotechnology companies within a State's borders, and the extent of involvement by universities and private industry. Although long-term, stable funding runs counter to the pattern of State investment, it is vital in the area of biotechnology. And States are uniquely situated to accomplish many technology transfer goals not easily attained by the Federal government because of the States' traditional role in economic development.

In the private sector, OTA found commercialization of biotechnology by U.S. industry to be healthy and competitive. OTA identified 403 American companies dedicated to biotechnology, and an additional 70 established corporations with significant investments in biotechnology. Combined, U.S. industry is spending an estimated $1.5 to $2.0 billion annually in biotechnology R&D.

Because biotechnology has become an essential tool for many industries, there is no such entity as "the biotechnology industry." Rather, biotechnology is a set of tools employed by several industrial sectors, each with its own advantages and obstacles in the race to market. Human health care, primarily therapeutics and diagnostics, continues to be the focus of most R&D investments, with chemicals ranking second and agriculture third as fields of application for industrial biotechnology (see table 3).

The boom time for the formation of biotechnology companies was in the period 1980 to 1984. During those years, approximately 60 percent of current companies were created, with nearly 70 new firms begun in 1981 alone. Consolidation within the industry and the predominance of a few firms has slowed that growth; nevertheless, the amount of money invested by larger, more diversified firms, such as the DuPont Corporation, continues to grow.

OTA found that strategic alliances between large corporations and smaller, dedicated biotechnology companies are increasing and are seen as a sign of financial strength by investors. Instability in the financial markets may accentuate the dependence of many smaller firms on large, established corporations. Most large corporations continue to rely on outside sources of innovation, either a smaller firm or a university scientist, with these collaborations benefiting both parties. However, the development of in-house expertise in biotechnology is occurring rapidly in major U.S. corporations.

OTA found that most industrial alliances occur between U.S. companies rather than between U.S. and foreign firms. The most common form of U.S.-foreign collaboration, when it does occur, is with Japanese firms, overwhelmingly in the application of biotechnology to human health care.

To date, dedicated biotechnology companies have raised over $4 billion from private investors, according to one estimate. Yet, 80 percent of that investment has been made in 10 companies. Investment in health care applications accounts for 75 percent of all investment. Agricultural applications have received only 16 percent of the total investment.

To illustrate the diversity of issues facing commercial biotechnology, OTA examined U.S. investment in biotechnology as applied to three specific industrial applications; human therapeutics, plant agriculture, and hazardous waste management. Biotechnology as applied to the development of human therapeutics represents an area where there has been substantial Federal support of basic research. As a result, the knowledge base is vast and growing, the commercial aspects enticing, and the regulatory regime similar to that applied to more traditional approaches of drug design and manufacturing. In the face of such promise, however, it is noteworthy that only eight human therapeutics using biotechnology have been approved for marketing in the United States.

In contrast, plant biotechnology faces a smaller knowledge base due to lower levels of Federal support for basic research in the plant sciences. The commercial applications in the field are less developed, although potentially profitable, and the regulatory framework new and evolving. Agriculture is a major contributor to the foundation of this country's economy. Research contributes significantly to its success, with an annual rate of return on investment estimated at between 30 and 50 percent. Biotechnology is expected to play a major role in strengthening this important part of the nation's economy. Its tools have the potential to modify plants to resist insects and disease, grow in harsh environments, provide their own nitrogen fertilizer, or be more nutritious. But success in this field is by no means assured. Many barriers must be overcome for U.S. agricultural products to remain competitive in world markets. The newer technologies can potentially lower costs and accelerate the rate, precision, reliability, and scope of improvements beyond that possible by traditional plant breeding.

Of all the problems facing agricultural research, the most pressing is the need for increased Federal support. In 1939, approximately 80 percent of federally sponsored research went to agriculture; by 1985 agriculture's share had shrunk to less than 2 percent. Moreover, only 1.4 percent of the Department of Agriculture's budget is devoted to research. In part, the advent of genetic engineering and related biotechniques has, itself, altered the shape and scope of U.S. agricultural research investment decisions. In particular, the emerging technologies present fundamental challenges and opportunities for the public component of U.S. agricultural research.

The application of biotechnology to waste disposal is still largely experimental, and the investment is small compared with efforts in pharmaceuticals and agriculture. Biotechnology's potential to remedy waste problems remains undeveloped due to a variety of technical, institutional, economic, and perceptual barriers. And, more so than in any other industry studied by OTA, the research agenda for waste disposal and pollution control is driven by regulation. The influence of the regulatory regime affects, to a large degree, the extent to which biotechnological applications have been studied. Regulation shapes the field of waste disposal and, thus, provides the impetus for efforts to develop new methods of pollution control. Yet fears of regulatory barriers are discouraging researchers from investigating genetic engineering as a way to discover potentially beneficial organisms.

Funding for research in this areas is insufficient and comparatively unstable. The Environmental Protection Agency is the lead agency in conducting research and development in waste disposal. But there is a near-consensus among scientists and industrial managers that EPA does not give appropriate weight to biotechnological approaches. The large initial investment needed to develop the appropriate technology, as well as the necessary knowledge base are obstacles to private initiatives. Small start-up biotechnology firms usually cannot afford the high financial risk required to achieve progress in the field.

In terms of overall employment in commercial biotechnology, the number of jobs has grown over the past decade. A 1987 OTA survey of U.S. biotechnology companies yielded an estimate of 35,900 jobs in the field, of which 18,600 are for scientists and engineers. Despite growth in employment in recent years, however, biotechnology is not expected to become a major industrial employer.

Although the supply of specialists in biotechnology appears adequate to meet current demand, shortages in particular areas will occur from time to time and are unavoidable. Demand for expertise in plant and animal tissue culture and protein chemistry may be outstripping supply, and a growing need for persons to assess the risks of engineered organisms released into the environment has led to a shortage of microbial ecologists.

The NIH, by far the largest Federal source of fellowships and training grants, is also the largest supporter of such training for biotechnology. Yet, the share of NIH's research budget devoted to training has shrunk from 18 percent in 1971 to a low of less than 4 percent in 1987. While NIH, USDA, NSF, and other Federal agencies provide substantial funds for research, which contribute indirectly to training, training grants, and fellowships are less well funded, and have declined in recent years. Training grants in particular areas of possible need, such as bioprocess engineering, plant molecular biology, and protein crystallography, could be given special consideration.

That concludes my summary of the principal findings of OTA's *U.S. Investment in Biotechnology*. The report identifies ten policy issues related to this topic that today confront Congress:

- appropriate levels of Federal funding for biotechnology research and development;
- required emphases on basic versus applied research;
- interagency cooperation in funding biotechnology research and development:
- information requirements necessary for coordinated and informed policymaking;
- Federal efforts in training and education for biotechnology;
- the effects of the Tax Reform Act of 1986 on firms commercializing biotechnology;
- export controls and biotechnology products;
- the need for guidelines for university policies on industry-sponsored research;
- Federal assistance for State efforts in biotechnology; and
- the adequacy of Federal mechanisms for assisting biotechnology firms in obtaining the financing necessary for start-up and scale-up.

I will briefly discuss several of these policy issues that are most relevant to the proposed legislation under discussion at these hearings.

An issue central to the findings of this report pertains to the adequacy of Federal support for R&D relevant to biotechnology. There are no objective and reliable measures for determining whether current Federal support for biotechnology R&D is sufficient. Clearly, intensive and sustained Federal investment in applications of biotechnology to the life sciences has been transformed into commercial products in some industries much faster than in others. Commercial applications are more advanced in areas such as human therapeutics, diagnostics, and chemicals than in plant and animal agriculture, or bioengineering for waste degradation. The slow pace of progress in the less developed applications of biotechnology is sometimes due to insufficient funds for basic research; while in other cases, potential products are simply not being developed because industry does not consider the biotechnology product or process sufficiently better (either functionally or economically) than those that already exist. Furthermore, excessive regulatory burdens or public perceptions associated with applications of recombinant DNA research can be more important factors than underfunding in some biotechnology applications, most notably in plant agriculture.

Anecdotal evidence suggests that the current system of research support in the United States sometimes fails to fill critical gaps between basic research related to biotechnology and development. Gaps could be filled through additional financial support for applied research, technology transfer, and increased Federal support for multidisciplinary research programs. Congress could direct Federal agencies to dedicate more of their budgets to applied and multidisciplinary research in biotechnology. Pressing needs for advanced R&D in specific industrial sectors may warrant a shift of emphasis in research support.

An issue raised in the OTA report concerns the need for more interagency cooperation in funding biotechnology R&D. While some redundancy and duplication of effort is an essential component of a healthy research enterprise, more formal cooperation between agencies in areas of shared interest could facilitate more rapid advances in some areas of biotechnology where there is insufficient or poorly focused support. Congress could establish an interagency coordinating body to identify areas of research that could be co-funded across agencies, address solutions to filling research needs, and develop strategies to promote technology transfer. At present, such coordination is rare and informal.

OTA found, in the process of producing this report, that information about Federal support for biotechnology research and training is scattered and inconsistent. Systematic evaluation of total Federal spending as well as direct comparison of spending in specific areas across multiple agencies is complicated by the definition of biotechnology employed by each agency as well as its method of accounting for expenditures. Regular and institutionalized reporting on levels of funding for research and training in critically important areas, such as biotechnology, could promote a more coordinated approach to setting strategies for biotechnology development.

Under The Federal Technology Transfer Act of 1986 (P.L. 99-502), directors of Government operated Federal laboratories may enter into collaborative R&D agreements with other Federal agencies, State and local governments, industrial organizations, and nonprofit organizations. OTA found that biotechnology is an area of research currently pursued in many Federal laboratories that could be more effectively shared with industry and universities through active compliance with P.L. 99-502. As one means of encouraging compliance with the intent of the law, Congress could request that agencies document the extent to which this has occurred within their laboratories.

OTA identified several issues pertaining to the effect of the Tax Reform Act of 1986 (P.L. 99-514) on firms commercializing biotechnology. Current provisions include: extension and reduction from 25% to 20% of the R&D tax credit; repeal of the investment tax credit for equipment investment; and abolition of the preferential treatment for capital gains. These provisions are expected to have a negative impact on the ability of small biotechnology companies to obtain funds for R&D.

An issue addressed in the OTA report focuses on growing concern that U.S. trade policy toward high-technology goods that could compromise national security poses a potential threat to the growth of biotechnology exports. A technical advisory committee within the Department of Commerce was formed in 1985 to address the question of biotechnology exports, but committee efforts to date have been marginal. As more and more biotechnology products become available for export, there is some concern on the part of industry that these products will become caught between the interests of Commerce and Defense, or will become delayed due to administrative confusion about the required approval process for biotechnology products. One option for investigating the approval process is to direct the Secretary of Commerce to evaluate the efforts of the Biotechnology Technical Advisory Committee. Without such evaluation, the economic potential of these technologies may never be realized if companies cannot comply with the procedures and restrictions associated with the Export Administration Regulations.

Finally, OTA reports that patent litigation in biotechnology is likely to increase given the complex web of partially overlapping patent claims, the high-value products, the problem of prior publication, and the fact that many companies are chasing the same products. How the courts uphold patents, and interpret new ones, as well as how well U.S. companies are able to protect patents abroad, will be issues facing the biotechnology frontrunners in the next few years. In addition, there are nearly 7,000 biotechnology patent applications pending at the U.S. Patent and Trademark Office. The PTO has experienced a turnover of and difficulty in acquiring patent examiners with expertise in fields associated with biotechnology. It has been taking 24 months, on average, before processing of a biotechnology patent application is initiated, compared with an average of six months for conventional drugs. This time lag, along with an atmosphere of general uncertainty over patent rights, may cause companies developing biotechnology products to file many more patents than are typical for conventional drugs.

In summary, several conclusions are apparent about the nature of U.S. investment in biotechnology. First, the level of investment is insufficient to meet the promise suggested by current work in the area. In particular, progress in such areas as agricultural biotechnology and biological approaches to waste disposal is hindered by inadequate investment by the public and private sectors. In both fields, technical problems exist because the result of incomplete knowledge of basic processes involving plants, micro-organisms, and microbial ecology.

Finally, biotechnology is a set of tools used in many industrial sectors. Each area of application presents a different set of issues for debate due to differences in the state-of-the-art, levels and proportions of public and private support, the effects of regulation, and the degree of commercialization in each area. As Congress discusses the various options by which to safely promote the growth of these industries, the diversity of issues facing these many sectors must be recognized.

Thank you for the opportunity to present OTA's analysis of ***U.S. Investment in Biotechnology.***

Table 1. — Federal Support for Biotechnology Research, 1985-1987
(current dollars in thousands)

Agency	fiscal year 1985	fiscal year 1986	fiscal year 1987
National Institutes of Health			
basic	1,208,229	1,202,094	1,388,337
applied	638,916	678,003	887,614
Total	1,847,145	1,880,097	2,275,951
Department of Defense			
basic	44,100	51,600	60,800
applied	48,500	49,000	58,000
Total	92,600	100,600	118,800
National Science Foundation	81,570	84,072	93,800
Department of Energy			
basic	45,500	45,000	50,100
applied	9,600	10,900	11,300
Total	55,100	55,900	61,400
USDA Cooperative State Research Service	48,000	46,000	49,000
USDA Agricultural Research Service	24,500	27,000	35,000
Agency for International Development			
broad definition	NA*	46,854	43,756
narrow definition	NA	14,332	6,082
National Aeronautics and Space Administration	NA	6,400	7,300
Veterans Administration	5,400	6,365	9,400
Environmental Protection Agency	3,000	3,400	5,666
National Bureau of Standards	850	3,300	3,300
Food and Drug Administration	3,000	4,700	5,800
National Oceanic and Atmospheric Administration	2,144	2,215	2,680
Small Business Innovation Research**	12,033	12,000	NA

* NA: Not available.

** SBIR dollars are a part of the total spending reported by the above agencies. They should not be added on to total spending.

SOURCE: Office of Technology Assessment, 1988.

Table 2. State Allocations for Biotechnology R&D, Training, and Facilities

State	FY 86	FY 87
Arizona	$1,170,000	$1,540,000
Arkansas	757,173	800,000
California	2,500,000	2,500,000
Colorado	500,000	500,000
Connecticut	665,000	1,100,000
Florida	5,050,000	7,050,000
Georgia	2,600,000	3,000,000
Idaho	438,800	450,000
Illinois	4,500,000	5,000,000
Indiana	4,000,000	1,029,904
Iowa	500,000	3,750,000
Kansas	162,000	172,000
Kentucky	908,500	896,600
Louisiana	670,000	NA
Maryland	2,600,000	3,900,000
Massachusetts	485,000	935,000
Michigan	6,000,000	4,000,000
Minnesota	1,032,000	1,100,000
Missouri	1,500,000	3,700,000
New Hampshire	150,000	450,000
New Jersey	10,000,000	35,690,000*
New York	34,300,000*	*
North Carolina	6,500,000	6,900,000
North Dakota	1,643,090	1,601,783
Ohio	2,194,787	50,000
Oklahoma	1,584,000	1,542,000
Oregon	350,000	360,000
Pennsylvania	2,848,824	18,035,494*
Tennessee	NA	800,000
Utah	110,000	500,000
Vermont	NA	300,000
Virginia	1,500,000	1,750,000
Wisconsin	190,000	418,000

NA: Not available.
* Indicates multi-year appropriation.
Source: Office of Technology Assessment, 1988.

Table 3. Areas of Primary R&D Focus by Biotechnology Companies

Research area	dedicated biotech cos. #(%)	large, established cos. #(%)
Human therapeutics	63 (21%)	14 (26%)
Diagnostics	52 (18%)	6 (11%)
Chemicals	20 (7%)	11 (21%)
Plant agriculture	24 (8%)	7 (13%)
Animal Agriculture	19 (6%)	4 (8%)
Reagents	34 (12%)	2 (4%)
Waste disposal/treatment	3 (1%)	1 (2%)
Equipment	12 (4%)	1 (2%)
Cell culture	5 (2%)	1 (2%)
Diversified	13 (4%)	6 (11%)
Other	31 (18%)	0 (0%)
TOTAL	296 (100%)	53 (100%)

Source: Office of Technology Assessment, 1988.

Mr. Scheuer. Thank you very much, Dr. Hanna, for your excellent prepared testimony and your remarks.

We have a roll call vote going on now, so we are going to suspend for approximately 15 minutes and then we will recommence with the remaining members of the panel.

[Recess taken.]

Mr. Scheuer. All right. The subcommittee will continue, and we will recommence with panel one, and we will hear next from Dr. Bruce Merrifield. Why don't you take 7 or 8 minutes, Dr. Merrifield, and hopefully chat with us informally.

Of course, for the benefit of all of you and all future panels, subsequent panels, your entire prepared testimony will be printed in the record.

STATEMENT OF DR. D. BRUCE MERRIFIELD, ASSISTANT SECRETARY OF COMMERCE FOR PRODUCTIVITY, TECHNOLOGY, AND INNOVATION, ACCOMPANIED BY DEPUTY ASSISTANT SECRETARY MICHAEL KELLEY, INTERNATIONAL TRADE ADMINISTRATION

Dr. Merrifield. Thank you, Mr. Chairman, and I would like to submit my written testimony for the record and then just make a few comments.

I am accompanied by Deputy Assistant Secretary Michael Kelley from the International Trade Administration, who has been responsible for developing these marvelous studies, industrial studies in this area, and he can help us with questions on trade policy if those arise.

You know, again I am very much impressed with your initiative here. Technology is the engine that drives all world economies. The pace of new technology is so great that it has collapsed life cycles in electronics already to 3 to 5 years, rarely more than 5 to 10 in most areas, and biotechnology will be no exception.

Basically, the rubric of our time is "innovate, automate, or evaporate," and we have to make sure that we have created the climate now in this country for the advancing technology that we uniquely have access to. I would like to stress that point because we have the most incomparable set of capabilities in this country to capture and retain and maintain technical leadership in any industry that any Nation has. We do spend about——

Mr. Scheuer. The question is, how do we keep it up and maintain our current preeminent position?

Dr. Merrifield. Indeed, that is true, and I think basically it is a problem of getting unnecessary barriers out of the way, providing specific incentives where those are needed, and I would like to address a few of those just briefly.

You know, again, you pointed this out: We have lost technology in certain areas. A classic example is the VCR. If we instead of the Japanese had spent about $500 million to develop that, we have calculated it would now be an $18 billion business and it would have contributed something like 140,000 jobs to the U.S. economy. That same thing happened with the RCA color TV and with robots, as you mentioned, and other areas.

Mr. **Scheuer**. I don't think we produce a single color television tube in this country any more.

Dr. **Merrifield**. We do, but not very many.

Mr. **Kelley**. No, as a matter of fact, we do produce a single color TV set. Panasonic makes it in Chairman Rostenkowski's district.

Mr. **Scheuer**. I'm glad to hear that, and it couldn't be located more salubriously. [Laughter.]

Mr. **Kelley**. And we have heard a lot about that.

Dr. **Merrifield**. Well, you know, the same thing could happen very easily in superconductivity. For example, the high definition television thing is an opportunity to recapture much of the consumer electronics business, if we could just get our act together there and provide the incentives and put together the collaborative efforts that are needed.

Those are big things that are beyond the individual capacity of individual companies to do alone, and some segments of the biotechnology area apply to that. Others do not, though. Of the 470 companies that we have in biotech now, many are doing, appropriately, their thing. They can do it alone, and we just need to make sure that we remove unnecessary barriers for them and provide incentives for them, and they can keep us at the leading edge.

There are other areas, however, like HD TV and superconductivity and the VCR, where perhaps a different mechanism has to be put in place. Agriculture, I think, is perhaps the classic example of this. For example, I think the agriculture situation is much worse than we tend to believe. It has been our major export business, $44 billion in 1981, down to $26 billion last year. Imports are up to $22 billion now.

Basically the reason for that is, all the developing countries around the world are using our technology—pesticides, fertilizers, herbicides, and so forth—to grow these commodity crops. China is now the world's largest exporter of wheat. The Campo Serado region in Brazil, with the equivalent of 10 midwestern States in area, two and a half growing seasons, will swamp the world in the next decade with low-cost food.

Mr. **Scheuer**. Well, to an extent, isn't—and I hesitate to interrupt, and I am sorry I am interrupting—but isn't that in some ways a healthy development, that the developing world is getting its act together as a major food producer? Doesn't that mean that maybe we should rethink our role as the wheat basket for the world and get our act together in terms of moving that role of simply raising wheat to a more high-technology, more skills, more science-intensive application of our particular American genius to do things that ought to be done, should be done, must be done, which they are probably not capable of doing? Maybe we have to look for a new role, other than being the wheat breadbasket for the world.

Dr. **Merrifield**. I couldn't agree more. That is exactly what I was about to say, the point being that what we have done now is, we have set up the Forest and Farm Products Task Force in the Department of Agriculture under Orville Bentley's leadership, and that task force has identified maybe 25 different plant species that, with genetic manipulation, could be improved in productivity and begin to diversify our agricultural base away from the commodity foods into proprietary, high-value industrial products that would make materials for industry.

Mr. SCHEUER. Now what do you mean by industrial products? You are still talking about food, aren't you?

Dr. MERRIFIELD. No, no, not necessarily.

Mr. SCHEUER. You are talking about products other than food and fiber?

Dr. MERRIFIELD. Absolutely.

Mr. SCHEUER. That could be raised on the farm?

Dr. MERRIFIELD. Absolutely. For example, the kanaf plant that makes these long fibers for paper, the jojoba plant that makes these excellent lubricating oils, the Auayule plant that makes natural rubber, those are well-known ones, but there are dozens of others that make very high-value products that have industrial potential for which other sources would not be as good. But the problem there is that no individual company can take the risk to do those by itself.

There is where the collaborative efforts and perhaps special incentive funding may be necessary if we are going to do that. I would like to differentiate that kind of thing from the gamma interferon, the growth hormone and so forth, that individual companies can do quite adequately by themselves.

The important thing, though, coming back to these big areas or these areas where there isn't an automatic constituency and an automatic risk available market, we need to address that problem. One of the great barriers that we have here in this country, and I wish I could really focus on this, is the high cost of capital. Our cost of capital and the availability of risk capital is a major barrier to the innovation process that we have in place but do not exercise.

Our cost of capital is at least three times higher here than in Japan. I think if you could really account for all the hidden subsidies that are involved there, they may have essentially a zero cost of capital and therefore zero risk in developing new things. They can take a long-term effort, make a long-term effort to develop these things which no individual company in this country could do alone.

Mr. SCHEUER. Excuse me again. There are two things about the Japanese genius for organizing their resources. First, they make capital available on much cheaper terms and, second, when they have gone through their analysis of what is important and what isn't and they decide to go for a winner, they don't go for losers. They don't spend their time subsidizing losers. They subsidize winners in areas that they identify as high priority areas, and when they do that, they are willing to wait. They will wait 10 years, they will wait 15 years before the first yen of profit shows up, if they are convinced this is an area that is going to reap enormous future rewards.

The owner of Japan's greatest machine tool manufacturing company told me how MITI, the Ministry of International Trade and Investments, met with him in the late sixties, and MITI targeted this company into the field of robotics. They laid out a plan, and it was perfectly clear they weren't going to make a nickel of profit for over a decade. They kept MITI very well informed of what they were doing. They had losses accumulating. Around the end of the first decade, the 11th or 12th year, they approached equilibrium, sort of broke even, and the 13th year they showed a little flow of water over the dam, and by the 14th year that little trickle had become a rush. Since then, they don't know what to do with their cash flow.

But they did it because they targeted this area and because MITI provided not only—of course, MITI didn't do it itself. MITI organized their banking system to provide this long-term financing. A, they came in with cheap money and B, even more important, they came in with patient money, and that is part of the Japanese genius. Our corporations tend to look at the bottom line not only on an annual basis but on a quarterly basis, and when it comes to doing the research and development that will produce enormous gains, but not perhaps for a decade or a decade and a half, the Japanese know how to do that. They know how to organize to do that and we simply don't, and this may very well be a critical area, a critical role where our Government can plan and should learn how to play.

Dr. MERRIFIELD. Well, I think that we have a better mechanism for doing this, that is better market-driven than that. In fact, the Japanese have made some rather serious mistakes in overbuilding capacity in steel and other commodity areas which now they have to write down, so they have not been perfect in their targeting. In fact, the market-driven strategies that we have developed, I think, are better.

In fact, since we got the antitrust laws changed, you know, in the Cooperative R&D Act in 1984, we have started up 79 major consortia now. There are about 25 more in the pipeline. There are over 1,000 companies involved in these. Sematech is one of the most recent ones, as you know, developing a 16 megabit flexible automated facility, $1 billion over the next 4 years. Not even IBM or Bell Labs could do that alone, but in collaborative effort they can do that.

But again, the risk there is very high in the sense that there is no assurance that other technology will not have intervened in that period, and so it takes collaborative efforts in these big-ticket things where individual companies don't have the risk tolerance to do it alone. That is where the low cost of capital, essentially no cost of capital, diminishes that risk for the Japanese. That has been our major barrier. Six to 8 percent real cost of capital is historically unprecedented, and it is awfully urgent now that we bring that down and make risk capital available, if we are going to mobilize these tremendous developments that we develop through our basic research.

Other barriers, of course, have been there, such as the antitrust laws, and I would like to point out that when Sematech develops this 16 megabit facility in a few years, they won't be allowed to operate because the antitrust laws don't allow collaborative manufacturing on that scale. That is ridiculous. We do have to further modify the antitrust laws.

You mentioned the process patents. Much of the economics of biotechnology will be in the process technology. Anybody can use our process patents at will, as you point out, and import back into the United States with impunity, pirating our basic technology there. It is important that we strengthen those process patents and prevent that pirating.

The Technology Transfer Act that we were talking about is probably the greatest act, the greatest privatization of Federal assets that has ever been made. It is finally releasing literally tens of billions of dollars of the world's most advanced technology for private sector commercialization, and it is as a result of that that many of these collaborative efforts now are forming between universities and companies, Government laboratories and companies.

Mr. SCHEUER. But you are suggesting we ought to go beyond simply permitting collaborative efforts in research and development, and actually go ahead and permit collaborative efforts in manufacturing, too?

Dr. MERRIFIELD. There is no question that we have to do that.

Mr. SCHEUER. Is this the official administration position?

Dr. MERRIFIELD. Indeed it is, and in fact I see much of the manufacturing that survives the next decade going to flexible, computer integrated systems, particularly for our second and third tier small suppliers to the major contractors. They are not competitive with offshore production, but with shared facilities which we are now beginning to put in place, they can be.

Just to give you an example, up in Meadville, Pennsylvania, near Erie, there are about 130 little machine tool people going down the tubes, and we have put together a consortium there of 24 of those who are pooling $15 million of their own money to put in place a four-module system, one for metal machining, one for plastic extrusion, ceramics processing, electronic assembly. They would all share that facility for just in time delivery of new things. It provides immediate entry into the marketplace for a new product or a modified product.

Basically it is transforming manufacturing, aggregating the manufacturing function into a service function where you buy time on the facility to make 1 or 10 or 1,000 of a kind at essentially the same cost, and making them competitive now with offshore production. The National Tooling and Machining Association wants to clone these things all over the country, where they can be satellite programmed to make whatever you need, where you want it, when you want it.

Well, this is the wave of the future, and the flexible automated systems now are one of our national priorities. We are currently working with about 45 centers around the country, mostly at universities because we see these as teaching facilities for the business school people, the engineers, the technicians that have to operate them. So the point is that, again, flexible manufacturing and shared flexible manufacturing is a necessity, and one of the barriers to that is the current antitrust laws that prevent them.

Mr. SCHEUER. Have you submitted proposed legislation to the Judiciary Committee?

Dr. MERRIFIELD. Yes. The superconductivity legislation contains a modification of the Cooperative R&D Act that would add "and flexible manufacturing" to it. I would hope that that could pass, and I think it is an urgent thing if we are going to be competitive in this area. Again, for example in biotech, there are some very interesting cases—of the 79 major consortia that we have formed, about 11 are directed to biotechnology. One of them, of course, is the Peoria biotech R&D consortium that involves the agricultural laboratory in Peoria with six firms that are now focusing on fermentation technology, which alone they feel they can't do.

So there are some good efforts here, and I think that is the model that we need to follow, but they are market-driven. They are driven by the private sector and they won't make the serious mistakes that some of the Japanese targeting strategies have done, where they have invested in areas that are now way overbuilt and they have to write those off.

So I hope that we can just accentuate the opportunities that we currently have. The cost of capital is a critical one, liability laws. There are certain regulatory barriers, particularly in the biotech area, that need selective modification, that are unnecessarily anticompetitive. Let's focus on removing those barriers, bringing down the cost of capital. We can recapture and maintain leadership in any industry if we just get our act together.

We have this incredible basic research that nobody else has; the greatest depth and diversity of industrial capability, 15 million companies in this country covering every known discipline. No other nation has that depth and diversity; an entrepreneurial culture that has permission to try and fail without personal social penalty, loss of face, an incredible advantage; the most flexible capital development capability; the world's largest market with a common language. We have everything in spades if we just get our act together.

I see the Government role, again, as a noninterventionist role that doesn't try to manage and direct these things, but can be a proactive agent of change that does remove barriers and does provide incentives, above all, helps catalyze collaborative efforts where those are necessary to recapture the industrial leadership.

Thank you.

[The prepared statement of Dr. Merrifield follows:]

Statement Of
D. Bruce Merrifield
Assistant Secretary Of Commerce for
Productivity, Technology, and Innovation

Before the Subcommittee on Natural Resources,
Agricultural Research and Environment
of the House Committee on Science, Space,
and Technology

July 14, 1988

Mr. Chairman and members of the Subcommittee, thank you for this opportunity to discuss the status of international competition and trade policy, particularly as they pertain to biotechnology products. My comments are in the context of your deliberations on H.R. 4502, the "Biotechnology Science Coordination and Competitiveness Act of 1988," and on S.1966, the "Biotechnology Competitiveness Act of 1987."

Accompanying me is Michael T. Kelley, Deputy Assistant Secretary for Basic Industries in the International Trade Administration (ITA). Basic Industries is the part of ITA concerned with biotechnology as well as pharmaceuticals and chemicals. You should direct any questions on competitiveness and trade policy to DAS Kelley.

I will confine my remarks here to some of the broader issues involving the commercialization of products flowing from research breakthroughs, such as those occurring in the biotechnology field.

First, let me emphasize that the U.S. has many advantages over other nations competing in worldwide market places. I realize that this statement flies in the face of some contemporary analyses, most of which tend to impart a negative flavor to our global economic posture. And, we do have a number of challenges to meet in upgrading our capacity to produce quality products at competitive prices. However, we must not overlook several unique factors which cast a most positive light on our competitive capacity. They include:

- a research and development capability that is second to none, with Federal and private sector expenditures exceeding $132 billion in 1987. Approximately one-half of all U.S. research and development is funded by the federal government. This funding accounts for approximately 80% of our basic R&D -- where breakthrough technologies like biotechnology occur. Compared to other countries, the U.S. still spends in absolute terms more on R&D than the next four largest western industralized countries combined (Japan, Federal Republic of Germany, France, and the United Kingdom). We produce more basic research than any other nation largely because of our excellent university and national laboratory systems. Federal funding for basic research overall increased 64 percent since 1981, while general science research increased 60 percent and engineering research 100 percent;

- the U.S. has the greatest breadth and depth of technical-industrial capability in the world to translate new discoveries into useful products, processes and services;

- the U.S. has a remarkable entrepreneurial culture which provides permission to fail and try again until success is achieved without permanent personal or public penalty;
- the U.S. has the largest pool of 4.5 million trained scientists and engineers in the world; and,
- the U.S. has the most flexible capital development capability in the world's largest financial market.

Secondly, the current explosion of advanced technology is creating unprecedented opportunities. Examples include:

- the development of advanced materials such as ceramics, super alloys, ultra-fine particle composites, and superconducting materials;
- the ever-advancing conquest of disease and the prolongation of life through the sequencing of the human genome leading to correction of genetic defects, and the progressive elimination of viral diseases; and,
- the discovery and production of synthetic enzymes, single function proteins, and other biotechnology advances that hold promise for conquering challenges as diverse as cleaning up hazardous waste sites and meeting worldwide needs for food, fiber, and fuel.

As the first "finding" in H.R. 4502 so aptly concludes, "biotechnology is an enabling technology which spans all sectors of the economy."

The overriding reality is that it is technology and its effective application to U.S. industrial and service sectors that will continue to be a main linchpin in U.S. competitiveness and, consequently, U.S. economic growth. The key point is that the United States, with its vast scientific and technological infrastructure and market, has the capability to be the world leader in practically any advanced sector. To do so, however, we must strengthen our primary long run comparative advantage -- knowledge and its application in continuously creative ways.

One of our greatest limitations in this regard is our comparative weakness in transforming research results quickly into high quality products and processes for the U.S. and other global markets. I am distressed that, a decade from now, our marvelous inventions in such areas as biotechnology and superconductivity may appear in the form of billions of dollars of foreign imports, yet in only millions of dollars for the U.S. in the form of royalty payments for the technology we invented but failed to commercialize ourselves. The VCR is a case in point.

Some of the criticism for this weakness must rest on short term U.S. business policies which do not have change adequately factored into them. There are companies which still see their business environments as static in an increasingly dynamic world. Simply stated, how can a business make the hundreds of tactical decisions required in any given year if it has no clearly articulated vision of where it must be to remain competitive in coming years? Strategies must reflect a future characterized by: continuous industrial restructuring; skill shortages, especially in the technical and managerial areas;

increased formal linkages with companies all over the world; and widespread use of flexible automation.

In all of this, the government role is to create a climate conducive to accelerated investments in innovation. For example, sound judgment and stability in monetary and fiscal policy is a must, as is financing for basic research. But we must also provide incentives, remove policy barriers, provide information and, where appropriate, supply catalytic services that individual businesses cannot supply for themselves. A primary focus of this should be in strengthening the effectiveness and efficiency of the technological innovation process, and in accelerating the conversion of the fruits of our research into commercializable products.

In terms of barrier removal, Commerce played a key role in the process that led to the passage of the National Cooperative Research Act of 1984. This modified U.S. antitrust laws to encourage cooperative R&D projects. To date, there are 79 consortia registered for the protection of the Act.

Of these, 11 are involved, directly or indirectly, with biotechnology and its techniques. The most prominent of these is the Biotechnology Research and Development Corporation (BRDC) in Peoria, Illinois. Six major firms, plus the Peoria Agricultural Research and Development Corporation are financing R&D in fermentation, working with the Department of Agriculture's Northern Regional Research Center at Peoria and the University of Illinois' Urban Biotechnology Center.

Through the Federal Technology Transfer Act of 1986, we cleared the way for a competitiveness-enhancing partnership between the private sector and our federal laboratories, such as the BRDC. This Act calls upon agency heads to allow their lab directors to enter into cooperative R&D agreements with the private sector, state and local governments, and universities. It also permits them to convey to business exclusive rights to inventions made by federal scientists, and establishes a royalty-sharing mechanism to reward the Federal inventors. Furthermore, consistent with Executive Order 12591, the Department of Commerce -- through its new Office of Federal Technology Management -- is working with the agencies and their laboratories to make the Technology Transfer Act as effective as possible. Already this office has developed model cooperative and licensing agreements.

Efforts by federal, state and local government to promote the development of our biotechnology industry inevitably center around universities and federal laboratories. Cooperation among government laboratories, universities and the private sector is vital if we are to successfully compete with countries like Japan. As I noted previously, we have long led the world in performing basic research. By strengthening the relationship between publically funded R&D and private sector development we are successfully balancing our scientific and commercial goals. The Federal Technology Transfer Act of 1986 has been a key initiative in advancing that process.

Turning to incentives, the Department of Commerce has taken the lead in several areas which deserve mention here. These are directed toward the objective of reducing the cost and increasing the availability of risk capital required for both innovation and automation.

Since 1981 we have promoted the use of R&D limited partnerships (RDLPs) which have funded an estimated $4 billion of R&D in recent years. While tax law changes have made this type of funding more difficult, it does continue today. There is an important feature about this type of funding that has motivated us to try to find ways for improving the old RDLP prototype. Of particular importance is the fact that RDLPs fund primarily product development -- a high risk part of the innovation process. That process comprehends the three stages through which a given product evolves from an idea/invention, through its translation and development, to its eventual commercialization. In the transition between the invention stage (where the product's technological feasibility is established), and the translation stage (where the product's development and interim manufacturing occur) there is a financing gap which is the weakest link in the whole innovation process. The RDLP is a particularly useful financing method to address that gap.

The biotechnology industry has taken great advantage of the two innovation funding devices that Commerce has promoted -- R&D limited partnerships (RDLPs) and cooperative R&D consortia. To quote a recent Arthur Young report based on a survey of 213 biotech firms, "It is probably safe to say that no emerging industry in history has been as adept at creative financing as has the biotech industry. Companies were founded with venture capital supported by collaborative arrangements and R&D limited partnerships -- all while waiting for the commercialization of the first products.

An additional catalytic type of service we render is to advise groups of firms -- on request -- on how to form R&D consortia.

We provide this help in the belief: (1) that risk is diminished through shared funding and skill pooling; (2) that accelerated development of next-generation technology may result; (3) that the productivity of U.S. firms' limited R&D budgets can be increased; (4) that these consortia can be a first step in the process by which U.S. firms will learn to cooperate with each other in R&D; and (5) that the very process by which these consortia organize themselves forces their member firms to develop long-term R&D strategies.

As another example of Department of Commerce work to promote biotechnology, our National Technical Information Service (NTIS) -- through its Office of Federal Patent Licensing (OFPL) -- has granted one hundred forty (140) licenses on biotechnology inventions in the last five years. The rate of licensing per year has been fairly constant at between twenty and thirty licenses issued. Of that, about 45% have been granted to small businesses.

The biggest single Federal license income producer in this area, during this period, has been the AIDS test kit which has generated in excess of $8 million in revenues for NIH.

My office also administers the selection process for annual recipients of the National Medal of Technology, which was established by the Stevenson-Wydler Act of 1980.

Tomorrow President Reagan will be presenting National Medals of Technology to ten eminent American technology pioneers. One of these is Arnold O. Beckman, a founding father of SmithKline-Beckman Corporation. Mr. Beckman is being honored for his exceptional creativity in designing analytical instruments that are recognized as some of the best in the world, and for developing a successful business whose products have helped to keep the United States in the forefront of biotechnology, chemistry and chemical engineering.

The International Trade Administration (ITA) carries out assessments of foreign government projects in biotechnology, performs market studies, and monitors industrial developments both in the U.S. and abroad.

ITA sponsors and participates in both national and international conferences that provide American companies the necessary exposure to meet international marketing challenges.

ITA is currently formulating long-range programs to help U.S. firms meet future marketing opportunities in Eastern Bloc countries.

Examples of recent activities include:

- Publications on biotechnology in Western Europe and the Pacific Rim countries (examples provided below) have been prepared. The information contained in these reports have been helpful to small biotech companies that are new to exporting.

- ITA has also sponsored U.S. participation at foreign trade shows and conferences to introduce U.S. biotechnology firms to those markets. For example, U.S. participation at the Hanover Biotechnica Fair has grown from 8 companies to 50 companies in the last three years.

- Recently, we sponsored a conference for State agencies interested in biotechnology. One of the objectives of that conference was to help coordinate State participation in overseas trade missions.

Also, the Patent and Trademark Office of the Department of Commerce has been involved in international negotiations to improve patent protection for pharmaceuticals and chemicals, including biotechnology products.

Selected publications by ITA as of July 11, 1988 include the following: Biotechnology in Western Europe (1987); Biotechnology in Singapore, South Korea and Taiwan (1988); The German Biotechnology Market (1988); JTECH Panel Report of Biotechnology in Japan (1985) (ITA and NSF); and U.S. Industrial Outlook chapter on biotechnology (annual since 1986). In preparation: Biotechnology in Japan.

In summary, the foregoing examples illustrate that the federal government has been steadily moving forward to try to create a favorable climate in which private sector innovation and product commercialization can flourish. Additional legislation -- or modifications to existing legislation -- are needed to reduce the anticompetitive aspects of liability laws, and to afford better protection of U.S. patents from foreign pirating.

However, we should never forget that real competitiveness happens at the marketplace level, keyed to the major elements of business competitiveness: quality, price, delivery time, and the ability to quickly adjust production facilities to meet new market needs. U.S. business must provide the strategic planning and leadership to knit our innovation process into a smoother working system. Private business must be the driving force to use our unparalleled technology base to seize market opportunities with new products and take a world view regarding the research we must perform and the technologies, product design, factories and products that we must develop to compete internationally in the future.

While the department supports the goal of H.R. 4502 and S.1966 -- that is, the establishment of a sound industrial and scientific infrastructure to foster competitiveness -- it does not support enactment of these bills because they duplicate ongoing activities. On balance, we believe they would probably impede rather than facilitate competitiveness in biotechnology. The creation of more commissions, panels, and boards as proposed by these bills would be counterproductive. The Departments of Energy and Health and Human Services will further explain this position. The establishment of a sound industrial and scientific infrastructure can not alone "create" competitiveness. That step remains the responsibility of our firms which then must convert the fruits of biotechnology science into usable products and processes for world markets. Without that private sector commitment, biotechnology will simply become another example in which we won the science battle, but lost the application war.

We have been advised by the Department of Justice that certain provisions of these bills present serious constitutional problems. That department will shortly be presenting its views on this issue to your Committee.

Mr. Chairman, thank you again for affording me this opportunity. I will be happy to answer any questions the Subcommittee may have.

Mr. SCHEUER. Well, thank you for that remarkable testimony.

Mr. Kelley, do you want to add some words to Dr. Merrifield?

Mr. KELLEY. Just a few words, Mr. Chairman. There may be a misperception here that the administration has been doing nothing about the commercialization of biotechnology over the last 8 years, and I think that is sort of a wrong perception. First of all, in 1983-1984 the Commerce Department, International Trade Administration, set up a biotechnology unit, and we recruited two individuals with science backgrounds but who also had an understanding of the commercial markets, and sent one to our embassy in London and sent one to our embassy in Tokyo to look at the biotechnology both in western Europe and in Japan.

Dr. Robert Yuan, who you are well aware of, was our person in London, eventually came out with the report which the committee has a copy of, or which we did send to you, called "Biotechnology in Western Europe." We also are in the process of doing the "Biotechnology in Japan" report, which should be out soon.

The original report, the original Government report, the major report on biotechnology, came out in 1984. It was called "High Technology Industries: Profiles and Outlooks." This was done by Emily Arakaki, who is an international trade specialist down in our area. We have also completed a report on biotechnology in South Korea, Singapore, and Taiwan, and we are presently targeting China and eastern Europe and updating the western Europe one.

This is all a way of saying that we have been gathering, for the last 4 or 5 years, a lot of commercial data, a lot of commercial background on what has been happening as far as international competitiveness in this particular industry, and what I would like to suggest to the committee, if and when they get time, is that we could come up with both Dr. Fugimora and Dr. Yuan and give a briefing on what these reports are saying and where we see this is happening. I don't think you have the time today, because we have a whole slide show and presentation that we can do, but we would be more than willing to schedule something with the committee if they would like to have that type of thing.

Mr. SCHEUER. Indeed we would like to have it. We would be extremely interested.

Mr. KELLEY. We would be glad to submit that for the record, if you would like.

Mr. SCHEUER. All right, in somewhat abbreviated form.

Mr. KELLEY. No problem.

Mr. SCHEUER. I think that would be very valuable, and we would appreciate that very much.

Mr. KELLEY. No problem whatsoever.

Mr. SCHEUER. And we will definitely schedule an appointment for Dr. Yuan to come down here.

Mr. KELLEY. Well, of course Dr. Yuan is a professor of microbiology over at the University of Maryland, and I can assure the Congressman, who is an alumnus of the University of Maryland, that those of us who are Georgetown alumni, we are preventing him from cloning any new basketball team over in that area. [Laughter.]

Mr. McMillen. I might add, you are doing pretty well for yourselves.

Mr. Kelley. One final statement, and then I will defer to questions. Last night you passed a trade bill, and I think as the committee considers this legislation that they are looking at, I think they have to look at the trade bill because one of the factors—and I have been around a little while in this town, too, and you have seen me in my other capacity as a lobbyist before, dealing with this committee on many issues—one of the problems that I see in this area is that we are passing legislation without looking at the international competitiveness aspect of what is happening in these industries.

If you look at that trade bill, and we are still looking at it, to be frank with you, there are a lot of questions in there on intellectual property rights, on changing the countervailing duties, on dealing with the administrative procedures on dumping, et cetera. These are very important to this particular industry, because as you talk of competition, you have to have, in order to prove dumping or to prove that there are unfair trade practices, you have to have facts and figures.

One of the areas which I would like to read for the record on this, and it is an area that I think should be considered, is the question of how do we get better data. One of the problems here is that we cannot really tell you what the actual figures are for sales of biotechnology or what our export position is, mainly because the Government through census is not collecting specific data on products of biotechnology or its exports. Biotechnology represents technologies and biological processes that are being applied in a number of industries, rather than as discrete products.

Therefore, sales data on products of biotechnology are being reported under broad industry groups, primarily pharmaceuticals and biologicals. Based on unofficial sources, we estimate that the sales of products made using recombinant DNA technology and monoclonal antibodies will exceed $900 million this year. In the next several years we expect the sales will be over $2 to $3 billion because of the influx of new products. Most sales will be accounted for by health care products over the next decade. Estimates for the year 2000 range between $10 billion and $40 billion.

The same data problem exists with the measuring of exports.

Mr. Scheuer. Excuse me. That is very interesting data on the future potential of that process. There was an article in the Wall Street Journal today. Did you read that?

Mr. Kelley. Yes.

Mr. Scheuer. It indicated this new biogenetic process that is aimed at a cure or a remediation for hemophilia could possibly hit $1 billion. If it is used not as a preventative but as a current curative, it is maybe less than half a billion if it is just curative, but if it is preventative and used more or less currently by hemophiliacs, by the hemophilic community, the market for that could be over $1 billion. When you think that we have estimated the total volume of the biogenetic market, so to speak, at $40 billion, and when you think that just this one product, just one single product in the medical field alone constitutes $1 billion, you can see that probably the

Japanese are far more on target with their estimate of $100 billion or more than we are with our U.S. estimate of $40 billion.

Mr. Kelley. I think that may be true, except that we are arguing on the side of conservatism at this particular point—no reflection on the administration, but we are arguing on that particular aspect. You are probably absolutely right, if the thing gets off the ground, but there are a lot of factors that will play into this, whether this market gets going or does not get going.

But one of the areas that I pointed out because it is very important, you guys did pass this trade bill last night, and you have to understand that we have the GATT negotiations going on, we have had the Canadian free trade negotiations which you will vote on later on this summer, and we have the trade bill which was passed. All three of those areas are major economic areas that have major, major, major implications on the future competitiveness worldwide of biotechnology. They will determine what the rules are in biotechnology, so whether it is $10 billion or $100 billion, those three areas are very important.

So as you look at this legislation, as you think about passing it, you have to look at those three areas and make sure they don't conflict with those areas. We did this in Superfund. When we passed Superfund legislation on that, we forgot what the heck the international competitiveness situation was in the chemical industry, our largest industry, which also was a major player, by the way, and is the major player in biotechnology. So we have to be careful as we legislate up on the Hill now, to understand that we are dealing in an international world. We are not dealing in a world here within these borders, so we have to be very careful of that.

That will conclude my statement, Mr. Chairman.

Mr. McMillen. I just have a quick question.

Mr. Scheuer. I am going to yield to my colleague, Mr. McMillen, in one moment, but I just wanted to tell you that it is unfortunate that the trade bill over the past months and even several years has been involved in some political controversy. It has gotten tangled up in politics, but let me assure you that we believe in unleashing the creative talent in our country in the field of biotechnology and enabling our country to compete in global commerce in biotechnology with the fetters off—in other words, providing the protection of the environment and health that we need, but then, after providing whatever environmental and health and safety protection is necessary and appropriate, then for the Government to provide some incentive, provide some stimulus, provide some direction and then get the bloody hell out of the way and not inhibit the genius in this country that has brought us to our present place of preeminence, which if it is inhibited is going to see us falling behind our competitors very rapidly.

Let me tell you there is no politics about this. There is a total bipartisan consensus, and I am sorry my Republican colleagues are otherwise occupied and overcommitted. I am sorry they are not here to express that, because I am sure they would agree there is no politics in liberating the biotechnology community to play a leadership role in global commerce.

Congressman McMillen?

Mr. McMillen. I just have a clarifying question for Mr. Kelley. You mentioned that the $700 to $900 million figure is current for the United States. Is that correct?

Mr. Kelley. That is correct.

Mr. McMillen. I have seen $700 million; you quoted $900 million. The $40 to $50 billion that you are quoting by the year 2000 is for the United States, as well. Is that correct?

Mr. Kelley. Yes, that is correct.

Mr. McMillen. Which really makes the point that when you look at industries around the world, and you realize you obviously are taking a more conservative posture on this, but if an industry does go from $700 million to $50 billion in 12 years, that is probably the greatest rate of return of any potential industry in this country, and it really makes the point that we do need the kind of coordination and strategy that the chairman's bill calls for.

I think the chairman's bill can also be very, very useful to sort through some of the points that you brought out about the trade bill and so forth. We need someone looking through this myriad legislation just to see where we are coming across obstacles that may impede our progress in biotechnology.

But I was just curious to clarify those statistics, that it is $700 to $800 million current, and the outside figure is somewhere around $50 billion by the year 2000, but you will take a range of——

Mr. Kelley. Yes, which would be, maybe as far as the current, maybe about $100 million in exports. You see, the problem is, we don't have the data. That was the other part of my area here, was that to obtain better data we have to have a special census survey, and we are going to have to figure out how to go in that area because it is very important. As much as we live in Washington and hate data, data controls a lot of the administrative procedures that you deal with in the international arena. You have to have data.

Mr. McMillen. I just want to understand the scope and the dimensions of it in the United States.

Mr. Kelley. Oh, yes. The chemical industry alone worldwide is about $356 billion. I know this because I testified 2 weeks ago before Senator Rockefeller's committee in Charleston, West Virginia, on the chemical industry, and the chemical industry is one of the, if not the major player in biotechnology. So if you have just got chemicals going—what?—at $356 billion now, and you figure that a lot of this biotechnology will eventually replace some of these chemicals or go in another area, you are talking about a big amount of money.

Mr. McMillen. Thank you.

Mr. Scheuer. Well, thank you very much for your intervention, Mr. Kelley. It was extremely helpful and very productive.

Okay, now we will hear the last witness on this panel, Dr. Yoshikawa. Please take 7 or 8 minutes or such time as you may need, Dr. Yoshikawa.

STATEMENT OF DR. AKIHIRO YOSHIKAWA, BIOTECHNOLOGY PROJECT COORDINATOR, BERKELEY ROUNDTABLE ON THE INTERNATIONAL ECONOMY, UNIVERSITY OF CALIFORNIA, BERKELEY

Dr. YOSHIKAWA. Mr. Chairman and members of the subcommittee, I would like to thank you for your invitation to participate in this important discussion of ways to promote biotechnology in this country. The Berkeley Roundtable on the International Economy is a university-based research think tank which specializes in the analysis of high-technology industries and international trade. We have been studying biotechnology as one of the key technologies for the future competitiveness of this country. I would like to briefly summarize some of our viewpoints.

Since I have 7 or 8 minutes, I would like to mention three things. Point one is, biotechnology is a crucial technology, strategically important technology to the U.S. Point two, Japan is in fact doing very well in this field. Point three is another question: Are we doing enough?

The field of biotechnology is having a profound effect on a wide range on industries. Its impacts are not only limited to a single product or a single industry. It will affect agriculture, pharmaceuticals and chemicals, as well as energy. Because it can affect so many different sectors in our economy, this is a key for the U.S. to maintain a competitive advantage in all these sectors, and this makes biotechnology a strategically important technology for the U.S.

The history of the American automobile and semiconductor industries is familiar to you all, yet only a few years ago America was dominant in these industries such as automobiles and semiconductors and machine tools, much as it is in biotechnology today. You may be surprised to learn of America's growing trade deficit with Japan in telecommunications equipment today. More alarmingly, a recent study indicates that Japan may already be ahead of us in the commercialization of superconductivity.

The question before us is whether America will permit biotechnology to go the way of these industries. While all these industries are in many ways similar to biotechnology, the stakes in biotechnology may be even bigger because biotechnology affects so many different sectors in our economy, and all these sectors will be affected by biotechnology. In the future, control of biotechnology may well prove to be equivalent to control of the core technology in the next industrial revolution.

America's lead in the biotechnology race may prove fragile. Japan's Ministry of International Trade and Industry, the so-called MITI, the champion of Japanese industrial policy, has already designated biotechnology as one of the key technologies for the future competitiveness of Japan. In the race to develop the next generation of biotechnology drugs, American and Japanese companies are locked in intense competition.

Genentech of San Francisco is the leader in the development of TPA, a heart attack medicine. However, today Japanese rivals such as Asahi Chemical are conducting phase 3 clinical testing in Japan. There is also widespread grassroots support for biotechnology in the Japanese public. When the Japanese cosmetic company called Kanebo introduced a biotechnology-based lipstick, widely publicized as a biotech lipstick, it proved a big commercial success. Another company called Kyowa Hakko marketed a new biotech wine called Fusion Bio A. Well, Mr. Chairman, you may not want to try this wine, but Japanese men and a growing number of Japanese women are now drinking biotech sake and biotech wine, and I believe——

Mr. Scheuer. I look forward, all of our committee on both sides look forward to testing this wine with you, Dr. Yoshikawa, and we want to do it in Tokyo where the product was developed. [Laughter.]

Dr. Yoshikawa. Okay. Well, I believe that Japanese people have a much more favorable view toward biotechnology-based products, and this may be a key to the successful commercialization of biotechnology in Japan, compared with the U.S.

The growing level of Japanese expertise in biotechnology is also evident from the development of biotechnology research supporting equipment, such as a sophisticated centrifuge and DNA sequencing machines. When I visited Japan several years ago, I went to one of the Japanese biotech labs, and much of that equipment was made in the U.S., made in England, or made in West Germany. A few weeks ago I went to one of the new Japanese biotech labs, and I was amazed to find that much of that equipment is today made in Japan.

I want you to remember the fact that before the explosive commercial success of Japan's semiconductor industry, there was a more subtle and largely ignored development in semiconductor manufacturing equipment, so I would say that Japan has now already established its foundation in biotechnology research and development and is ready to go much faster.

Even though many have concluded that Japan is a distant second to the U.S. in biotechnology, I disagree. Competitive advantage is a dynamic concept. It is not a static concept. With strategic policies and a commitment to move on for the next 15 years, even if you are losing some money for the next 5 or 6 years, with those commitments Japan may in fact come out as the front-runner, not second.

Well, let me briefly summarize Japan's industrial policy in support of biotechnology, because this may be relevant to this discussion here. The year 1981 was said to be the year the new biotechnology was born in Japan. The Ministry of International Trade and Industry introduced a comprehensive industrial policy to promote this new biotechnology.

In 1985 MITI established the Protein Engineering Research Institute and invited several companies from different industrial backgrounds: a computer software company, as well as hardware chemical and pharmaceutical firms. It is said that the study of protein structure is crucial for the development of the next generation of biotechnology drugs. In 1986 the Ministry of Health and Welfare established the Human Science Foundation, to promote the cooperation of private companies, universities, and government in the development of new pharmaceuticals.

America, by contrast, has several significant difficulties or challenges in formulating successful policies to support its competitive position in biotechnology. Even within the private sector, it is very difficult to form a consensus between small biotechnology companies and well-established, large chemical and pharmaceutical companies, also involved in biotechnology but with very, very different needs. Without such a consensus and with possible conflicts of interest among large and small companies, it will be very difficult to develop and coordinate a comprehensive, long-term industrial vision.

U.S. corporate financial practice makes it difficult for management to sustain short-term financial losses in order to expand and maximize future profit potentials. The structure of the American corporate financial system is oriented toward short-term profit, and makes it very difficult to make a commitment for the next 10 or 15 years. We are talking about the pharmaceutical industry, the chemical industry, and agriculture in the year 2000. It is 15 years ahead of us.

Let me tell you one story about semiconductors. In 1979 we had a second oil crisis, most American companies decided to cut down their investment in manufacturing facilities, but the Japanese Government realized that the semiconductor is a key for the next generation of industry, so they just kept on investing. They kept their investment in the semiconductor industry in Japan. Now we are talking about a 15-year commitment, not a one year or even one quarter commitment. In order to realize a comparable long-term commitment and in order to develop a long-term strategic viewpoint, I think it is very important for this Government to establish a coherent and comprehensive policy to support biotechnology.

I believe both H.R. 4502 and S. 1966 are an important first step toward realizing an effective American biotechnology policy. However, I cannot help but feel that both are overly vague. The more difficult the hurdle for us, the more difficult the question is of how to implement this policy and make it work well. The vagueness of both bills may indeed reflect the lack of consensus I mentioned already in the U.S. biotechnology industry.

The idea of establishing an advisory panel on this issue is a sound one. However, given the diversity of size and expertise among American companies, I am not too confident that such a panel can come up with coherent strategic recommendations. Nevertheless, I recommend that representatives from the private sector be given a greater leadership role in the formation of such an advisory panel. Established chemical, pharmaceutical, and other biotechnology related companies, as well as smaller yet commercially successful leading biotechnology companies, should be represented.

I understand that this is a time of severe budgetary constraints. However, we must remember that this sort of investment in an industry of the future will have great benefits to our children. Unless America can respond to this challenge from the Japanese and challenge from the Europeans, the future benefits to our children will be diminished. I support, again, both H.R. 4502 and S. 1966.

Thank you.

[The prepared statement of Dr. Yoshikawa follows:]

STATEMENT

OF

AKIHIRO YOSHIKAWA, PH.D.

BIOTECHNOLOGY PROJECT DIRECTOR
BERKELEY ROUNDTABLE ON THE INTERNATIONAL ECONOMY
UNIVERSITY OF CALIFORNIA AT BERKELEY

TO

THE SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE, RESEARCH
AND
THE ENVIRONMENT
OF THE
COMMITTEE ON SCIENCE,SPACE, AND TECHNOLOGY
U.S. HOUSE OF REPRESENTATIVES

ON

JULY 14, 1988

Mr. Chairman and members of the subcommittee, I would like to thank you for your invitation to participate in this important discussion of ways to promote the development of biotechnology in the United States.

The Berkeley Roundtable on the International Economy is a university-based research institute which specializes in analyses of high-technology industries and international trade. We have been studying biotechnology as one of the crucial technologies for the future competitiveness of the U.S. I would like to briefly summarize some of our view points.

Biotechnology: A Strategic Technology

The emerging field of biotechnology is having a profound effect on a wide range of industries. Its impacts are not limited to a single product or industrial classification, but range from agriculture to pharmaceuticals. Through the use of biotechnology, traditional agriculture may be transformed into a new engineering-based "manufacturing" industry. Today in Japan, traditional manufacturers of sake and other manufacturers in food processing are transforming themselves into high-technology companies. Combining biological functions with microelectronic technologies may also establish a new field of bioelectronics. Because it can affect so many sectors in a national economy, biotechnology is becoming a crucial factor for maintaining a competitive edge internationally.

At the moment, biotechnology is one high-technology sector in which America retains a technological advantage over rival nations such as Japan. The rDNA technique was invented in American labs, the products were first commercialized by American companies. The history of the American automobile and semiconductor industries is familiar to you all. Yet only a few years ago America was dominant in industries such as automobiles, semiconductors and machine tools much as it is in biotechnology today. You may be surprised to learn of America's growing trade deficit with Japan in telecommunications equipment. Where did we lose our technological superiority in telecommunications technology? The deregulation of ATT without consideration of the international competition may be at least partially responsible. More alarmingly, a recent study indicates that Japan may already be ahead of the U.S. in the commercialization of new materials, including super-conductors.

The question before us, then, is whether Americans will permit biotechnology to go the way of these other industries, born in the U.S. and captured by other nations. While all of these industries are in many ways similar, the stakes in the biotechnology race may in fact be higher than in any of the others. Given biotechnology's immensely broad range of possible applications, in the future, control of biotechnology may well prove to be equivalent to control of the core technology in the Third Industrial

Revolution.

The Overall Competitive Position of the U.S. in Biotechnology

America's lead in the biotechnology race may prove fragile. Japan's Ministry of International Trade and Industry (MITI), the champion of Japanese Industrial policy, has already designated biotechnology as one of three key technologies for Japan's future. Small, start-up American biotechnology companies with limited economic resources are competing against larger and more diversified Japanese conglomerates actively supported by the Japanese government.

In the race to develop the next generation of biotech drugs, American and Japanese companies are locked in intense competition. Even though Genentech is the leader in the development of TPA, a heart-attack medicine, Japanese rivals such as Asahi Chemical are also conducting Phase III clinical testing for TPA in Japan now. In the development of another biotech drug, SOD (Superoxide dismutase) which could be the next biotech block-buster, I believe that the Japanese are ahead of American rivals.

There is also widespread "grass-roots" public acceptance of biotechnology in Japan. When the Japanese cosmetic company, Kanebo, introduced a biotechnology-based lipstick, widely publicized as a "biotech" lipstick, it proved a big commercial success. Another company, Kyowa Hakko, marketed a new "biotech" wine, called "Fusion Bio A". Japanese women are using biotechnology-based products on their lips, and Japanese men (and a growing number of Japanese women) are drinking biotech wine. I believe that Japanese people have a much more favorable attitude toward biotechnology-based products, and this may be the key to Japan's success in commercializing biotechnology.

The growing level of Japanese expertise in biotechnology is also evident from the developments in research equipment supporting biotechnology, such as a sophisticated centrifuge and DNA sequencing equipment. When I visited a biotechnology lab in Japan several years ago, almost all the research equipment was made overseas. This year I again visited a new biotechnology lab, and was surprised to learn that much of the equipment is now made-in-Japan. Before Japan's explosive success in semiconductors, there were subtle and largely ignored developments in semiconductor manufacturing equipment. I believe that Japan has now completely established its foundation in biotechnology R&D.

Even though many have concluded that Japan is a distant second to the US in the biotechnology race, I disagree. Competitive advantage is a dynamic, not a static, concept. With strategic policies and the will to sustain short-run financial losses for future profits, Japan may in fact come out as the front-runner.

Japanese Industrial Policy in Biotechnology

Let me briefly summarize Japan's industrial policy in support of biotechnology, since it may be relevant to our own efforts to formulate an effective government policy in the U.S.

The Japanese government has introduced various mechanisms, both old-fashioned and experimental, to foster the country's success in biotechnology. Because biotechnology will affect a wide range of industries, several ministries have introduced separate (although often overlapping) policies to promote such research.

In 1984, the Ministry of Agriculture, Forestry, and Fisheries (MAFF) organized a basic research group on cell fusion, with 14 firms joining the group. The ministry is trying to develop biotechnology-based crops in cooperation with private firms. In 1986, the Ministry of Health and Welfare (MHW) established the Human Science Foundation (HSF) to promote the cooperation of private companies, universities, and government in the development of new pharmaceuticals.

The Ministry of International Trade and Industry (MITI) has overseen various efforts to carry out basic and applied research in biotechnology. The Next Generation Project was established in 1981 to promote the three "key" technologies for the future: next-generation microelectronics, new materials, and biotechnology.

To coordinate joint research in biotechnology, the Biotechnology Research Association was established and subdivided into three groups. Each group's research was designed to be conducted in close cooperation with government research institutions, such as the Fermentation Research Institute, the Research Institute for Polymers and Textiles, and the National Chemical Laboratory.

Close examination of the members of the joint research association provides an interesting observation. Many of the firms involved in the joint research association are chemical companies. The chemical industry in Japan is often characterized as a "declining" industry. We therefore see an interesting mix of industrial policies to promote next-generation industries (the sunrise industries) and to reinvigorate declining industries (the sunset industries). This policy mixture may imply a strong government commitment to transform the declining chemical industry into a sunrise industry once again. With these forms of government support, the chemical companies are likely to make substantial investments in biotechnology. Whereas public policy in the U.S. has emphasized the formation of new companies to promote biotechnology, Japan has tried to transform existing companies in assisting the smooth adaptation of biotechnology.

Recently, MITI introduced a new framework for cooperative R&D. The Key Technology Center was established in 1985 with the Ministry of Post and Telecommunication (MPT) by utilizing a fund made available from the sale of NTT (Nippon Telephone and Telegraph) stock. Under the Key Technology Center scheme, two or more firms acting on their own initiative can jointly establish an R&D company and conduct research. R&D companies are established through joint investment by the Key Technology Center and by member firms. The Key Technology Center provides up to 70% of the investment necessary for the joint venture.

Four companies related to biotechnology were established with financial support from the Key Technology Center. In 1985, five private companies (Toray, Mitsubishi Chemical, Kyowa Hakko, Takeda Chemical, and Toa Nenryo Kagaku) jointly established the Protein Engineering Research Institute (PERI) to conduct research in protein engineering. Nine additional companies (Kirin Beer, Suntory, Nippon DEC, Nippon Roche, etc.) later joined the PERI. It is said that the study of protein structure is essential to promoting the next generation of pharmaceutical products. The total investment in the PERI is expected to be 17,000 million yen (about $115 million) in 10 years.

In 1986, two other R&D companies were established. One was PCC Technology, which was jointly created by Kyowa Hakko, Mitsui Petrochemical, Kirin Brewery, and other firms to conduct research on plant biotechnology. The second one, the Foundation of Biomaterial Research Institute (BRI), was created by Toray, Sumitomo Bakelite, and Sumitomo Electric. BRI was established to develop bioactive materials by hybridizing synthetic materials and living cells to produce artificial organs and biochips.

Although Japan has been praised for successfully developing superior process technology, it has been argued that the country has proven to be neither original nor innovative. It is widely believed that Japan is better at improving or modifying existing technologies than at creating new technologies. In order to promote original research, Japan's Science and Technology Agency (STA) introduced new projects emphasizing interdisciplinary approaches to science: Exploratory Research for Advance Technology (ERATO) and the Frontier Research Program. STA is the foremost governing body of Japanese science and technology policy with the primary function of promoting basic scientific studies.

Difficulties and Challenges in the U.S.

America, by contrast, faces several considerable difficulties or challenges in formulating successful policies to support its competitive position in biotechnology. Even within the private sector it is difficult to form a consensus between the small biotechnology-specific start-up companies and the large, established chemical and pharmaceutical companies also involved in biotechnology but with very different needs. Without such a consensus and with possible conflicts of interests among large and small companies, it will be very difficult to develop and coordinate a comprehensive long-term industrial vision.

American industries are also generally much less likely to work closely and effectively with their government than are their Japanese counterparts. Perhaps as a result, issues such as international competitiveness and industrial survival are rarely brought into consideration when formulating the diverse range of government policies that ultimately have an impact on an industry as broad in scope as biotechnology. FDA and health care financing regulations, for example, that treat biotechnology drugs equally with conventional counterparts do not consider the long term economic (and medical) potential of this new and relatively vulnerable industry.

U.S. financial practices likewise make it difficult for management to sustain short term financial losses in order to expand and maximize future profit potential. Financially, biotechnology is not a low-risk investment, and companies must invest years in advance of any significant returns. The structure of the American financial system (oriented toward short-term profits) therefore makes it even harder to form a long-term vision for the industry, and invest in new products even when no immediate profits are in sight.

H.R. 4502 and S. 1966

I believe that both bills H.R. 4502 and S. 1966 are important first steps toward realizing an effective American biotechnology policy. However, I cannot help but feel that both are overly vague. The more difficult part for us will be implementing such a policy and making it work well. The vagueness of both bills may indeed reflect the lack of consensus I mentioned above in the U.S. biotechnology industry.

The idea of establishing an advisory panel on this issue is a sound one. However, given the diversity of size and expertise among American companies, I am not confident that such a panel can come up with coherent strategic recommendations. Nevertheless, I recommend that representatives from the private sector be given a greater leadership role in the formation of such an advisory panel. Established chemical, pharmaceutical, and other biotechnology-related companies as well as smaller yet successful leading biotechnology companies should be represented.

I also believe that more federal funding should be allocated to joint R&D taken among private companies. One Japanese example we may draw upon is to establish an institute to study protein engineering. Such an institute should be formed among companies in the chemical industry, computer software and hardware, pharmaceuticals, etc., in order to pool different industrial expertise. Exemption from potential antitrust litigation for federally sponsored joint R&D may be equally useful.

While I realize that this is a time of severe budgetary constraints, we must remember that this sort of investment in the future of an industry will have important long-term financial payoffs in tax revenue alone far beyond the value of the initial investment. In the biotechnology race, America's economic national security is at stake. Unless America can respond to the Japanese challenge with a comprehensive, coherent, and effective policy of her own in support of biotechnology research, American companies will be functioning at a serious disadvantage against their Japanese rivals in this crucial industry.

Thank you.

Mr. SCHEUER. Well, I can't thank you enough for your outstandingly helpful and fine testimony, Dr. Yoshikawa. Let me say, on the question of vagueness, there isn't a consensus yet but we hope that the commission will forge that consensus, and that is why we were a little bit vague deliberately, but we will be conferring with you privately and it may be that we should sharpen up some of the definitions there, and perhaps sharpen up the process.

Let me also say that you have hoisted up the early warning signal to us, and if we ignore it, we ignore it at our peril. It is true that we are in a time of economic austerity and we have to make an attack on that budget deficit. There may be areas in our society where we can afford to cut, but it seems to me we cannot afford not to move ahead in this area of biotechnology, as you have indicated. Unless we have a commitment to organizing our resources over this kind of 10 or 15-year time scale that you have pointed out, we are going to be breathing Japan's exhaust fumes in this whole area, and those of Europe, too, because we failed to establish priorities and because we failed to produce the national will and commitment to do the job, just exactly as you have stated, so if we ignore your warning, we do it at our peril.

All right. I am going to yield now for questioning to the co-chairman of this hearing, Congressman Doug Walgren of Pennsylvania, for questions, and he will chair the next panel, and then I will come back and chair the last panel. I yield now to the co-chairman of this hearing, Congressman Doug Walgren of Pennsylvania.

Mr. WALGREN. Well, thank you very much, Mr. Chairman, and let me say, as I have had to say so often, that the instinctive cooperation between the two subcommittees that Congressman Scheuer and myself are involved in, I think the world of and want to express my appreciation for. The more breadth of involvement we have on the Science, Space, and Technology Committee between subcommittees, I think the stronger can be our response, and I appreciate Mr. Scheuer's including us in as a subcommittee. The members on my committee are very interested in this area.

Let me ask where we are on this, on the question of these patent backlogs. I suppose it is a question that perhaps several of you might want to comment on, and I apologize for not being here earlier. If it has been covered, please short-circuit it, but it just seems to me that obviously the engine of our system is in the right to property, and if we are not getting that right out there in a reasonably quick fashion, then we are really handicapping the development of American industry and the strengthening of the investment in the area in particular, so how is it that we face 7,000 patents not being processed at this point?

Mr. PRICE. Mr. Chairman, will the gentleman yield?

Mr. WALGREN. I would be happy to yield.

Mr. PRICE. I would like to just underscore the importance of that question. We have had hearings earlier in the spring in the Small Business Subcommittee on Regulation and Business Opportunities, and heard at great length about that patent backlog and heard numerous suggestions for dealing with it, everything from more and better-trained examiners to streamlined procedures, so I do think that is an important question and I am glad that we can pursue it here.

Dr. MERRIFIELD. Well, maybe just a couple of comments here. First of all, the Patent Office has been inundated with these applications, many of the them from Japan. Some people have suggested that is a strategy to create a problem for issuance. I am not sure that that is——

Mr. SCHEUER. To bog down the Patent Office?

Dr. MERRIFIELD. That is correct, and the problem again is the fact that we don't have adequate numbers of trained examiners there to deal with this, and the automated systems yet in place that would facilitate the process of search. Now that is going on, and hopefully within another couple of years we will have the automated systems that will facilitate this type of process.

A number of companies, of course, have offered to provide their own people to help in this process, but there is a conflict of interest possibility there which makes that a difficult solution, and so it is not an easy problem. This is a very active area and I think we can expect a continuing inflow of patent applications, and it is something that we have to address.

The critical problem, again, is trained examiners that are qualified to really search out and make these decisions. Again, I think we really have to defer the full understanding of this to the Commissioner of Patents, Don Quigg, who can be more knowledgeable about what plans he has in place to do something about it.

Mr. WALGREN. Could I ask—you say that a large number of these are foreign applications—what is the balance in this area between American applications and those coming from abroad?

Dr. MERRIFIELD. I don't know what the numbers are, but basically the Japanese strategy is to blanket a given area with a lot of little picket patents which would never see the light of day in our system, and will not, probably, but they do inundate the system. In Japan they allow those, you know, superficial things like the clamp that holds a piece of equipment together and things like that that are obviously not valid inventions at all, but tend to block access or operations of our technology in their country, for example, even though we have the basic patents, and so there is a strategy here that is involved that is really bogging down the whole system, and we have to find ways to begin to cope with that. It is not an easy problem.

Mr. WALGREN. Other comments? Mr. Kelley?

Mr. KELLEY. Well, the other problem is that, besides biotechnology, we are starting to get inundated on superconductors, on the advanced materials in some of the areas that we talked about maybe two weeks ago, on metal technology. All that type of area is also going in, so your biotechnology isn't just the roadblock there. There are a heck of a lot of other high tech areas.

Dr. MERRIFIELD. That's true, exactly 1,500 patents on superconductivity, again many of them trivial that won't ever see the light of day, but they still have to be addressed, each one individually.

Mr. WALGREN. Can you give us some measure of the comparative investment in the private sector between the United States and Japan and the other players?

Dr. MERRIFIELD. Yes. We are currently spending about $4.7 billion a year in biotech.

Mr. **Walgren**. Total U.S. spending, Government and private sector?

Dr. **Merrifield**. That's right, $2.7 for—these are your numbers—$2.7 billion for the Government, about $2 billion in private sector companies, 470 companies. By comparison, the European investment is about $800 million, and I think $860 million for Japan at the present time. We are presently spending maybe five or six times more here than they are in biotechnology. Some of it, of course, is redundant effort.

Mr. **Walgren**. And what about the expenditures in the engineering centers? The NSF has some engineering centers that are focused in that area, as I understand it. The last witness mentioned a protein engineering center that the Japanese have developed. How do we compare on that kind of—I guess it is a focus, a technology focus, as opposed to just investing in biotechnology as a whole?

Dr. **Merrifield**. I think I will ask Kathi to give you the numbers, but this is an important point because the economics of the biotech area are largely going to be in the process technology, the fermentation and separation technologies. That is where the Japanese have been focusing because they understand that that is where the economics are. So they can wait around for our 400 little companies to come up with their new developments and undercapitalize, provide the capital for or acquire that technology and feed it into their automated systems in fermentation and separation.

Again, our process patents are vulnerable here, again because any country in the world can pirate them at will and use our technology, set out in our own patents, and then import back in the United States. This is why strengthening the process patents is so critical.

Kathi, do you have some comments here?

Dr. **Hanna**. The only formal Government-funded collaborative effort between university and industry comes out of NSF, the Bioprocess Engineering Center at the Massachusetts Institute of Technology. That is funded at a level, total Federal funding, of approximately $3.5 million; most of that coming from the NSF with some training dollars coming from the NIH. The Federal funding for that center is due to be withdrawn in 1990, at which point the center is supposed to be self-sufficient, either raising funds on its own through its usual grants program or through industry sponsorship.

There is considerable concern from people at the Center about their ability to raise those funds and to become self-sufficient; the first concern being that they rely on their scientists to raise the money. This creates great frustration on the part of the scientists who are not able to do their research, and also are not used to doing this kind of thing. The second issue has been that if MIT is having problems in gathering industry sponsorship, that does not bode well for other institutions that might not have the same reputation. I think NSF is looking at their ERC program, and that is really the only model we have to look at right now.

Mr. **Kelley**. This also points up to the need for the upcoming Uruguayan round negotiations on GATT, because one of the major provisions in these negotiations will be intellectual property rights. Unless we can establish that worldwide, what Secretary Merrifield talks about here, we are going to have a lot of problems. That is why the pharmaceutical and the chemical industries are so interested in the intellectual property rights section.

Mr. WALGREN. Thank you, Mr. Chairman. Mr. Chairman, was I under direction to recognize the gentleman from Maryland next? I don't mean to——

Mr. SCHEUER. When my co-chairman is finished with his questions, I will recognize the gentleman from Maryland.

Mr. WALGREN. I yield back the balance of my time.

Mr. SCHEUER. Only if you are finished with your questions. Are you finished?

Mr. WALGREN. Yes.

Mr. SCHEUER. Okay. The gentleman from Maryland.

Mr. MCMILLEN. I just have a quick question or two because I know my colleague from North Carolina wants to do so, and we may have a vote any moment. I would just like to generally ask the panel to respond to this in a general sense. In regards to H.R. 4502, the establishment of a national advisory committee, do you think that the national strategy that is being devised by this committee will help us be more competitive, or on the contrary that this master plan might in fact preempt free market forces? I am asking kind of a devil's advocate question because some in the administration would view this kind of industrial planning as anathema to free market forces, and I would appreciate your comments on that, particularly Dr. Merrifield, if you don't mind.

Dr. HANNA. I think that one of the issues raised in the OTA report deals with whether, if you look at Federal funding of basic research, this type of a cross-agency or commission would at the very least be able to operate within the Federal Government, the Federal research structure, in trying to perhaps spend money more efficiently. I think that what industry spokespersons told us during the report was that this kind of a commission, were it not to have too much authority, would be able to at least signal priorities and send messages to both the public and the private sector about the importance of certain things.

Mr. MCMILLEN. Dr. Merrifield?

Dr. MERRIFIELD. Well, I have sort of mixed feelings about it. You know I always am very appreciative of input and advice. The critical thing in almost every situation is the data base, and the continuing data base that Mike pointed out is so critical. This is why the OTA study is so important. It really sets out a lot of the current facts from which we then can depart in terms of options and pros and cons and so forth. Without that data base, we are always talking at odds and ends with each other, with misinformation and disinformation involved, so the competitive assessment is a critical thing.

To the degree that such a committee might provide that ongoing competitive assessment, it could contribute. On the other hand, we are doing that. Mr. Kelley is——

Mr. SCHEUER. Excuse me. Do you mean commission? Are you talking about the proposed commission, Dr. Merrifield?

Dr. MERRIFIELD. Yes, right.

Mr. SCHEUER. I want to just correct the record. It is a commission, not a committee.

Dr. MERRIFIELD. I'm sorry, the commission, yes. So its contribution could be effective if it were properly structured. Alternatively, what it tends to do, as far as I read the thing, is sort of redundant in terms of what is already going on here and here, and could even be——

Mr. SCHEUER. For the record, could you tell us what "here" and "here" means?

Dr. MERRIFIELD. Well, the OTA studies that are very, very well done, and of course the ITA studies focused on the industry level, so I think that if we have a commission of this sort, it ought to have a clear understanding of what its responsibilities and opportunities and limitations are, so that it doesn't contribute to the confusion but rather contributes to something that is positive.

Mr. MCMILLEN. I am going to stop there so I can turn over to my colleague so that he can ask some questions. I have a few more questions that I would like to submit, some of them, later on; but one last quickie, just give me 30 seconds on it. In your view, across the board, is the cost of capital issue, what Dr. Merrifield mentioned, the number one impediment to the growth of biotechnology in this country, internationally? Would that be viewed as number one? Just give me a yes or no on it.

Dr. YOSHIKAWA. Well, cost of capital is one but I think——

Mr. MCMILLEN. Is that number one?

Dr. YOSHIKAWA. I would say number one is a long-term commitment on the vision.

Mr. MCMILLEN. Dr. Kelley?

Mr. KELLEY. I would say there are two, capital and regulatory.

Mr. MCMILLEN. Dr. Merrifield?

Dr. MERRIFIELD. Well, both of those are critically important.

Mr. MCMILLEN. Ms. Hanna?

Dr. HANNA. I really can't form an opinion on that.

Mr. MCMILLEN. Mr. Chairman, I am going to defer to my colleague from North Carolina.

Mr. KELLEY. Could I just say one thing on the committee structure area, or the commission structure? The problem sometimes in these commission areas, especially when you are dealing with high technology—and this has just been our experience looking at it in the advanced materials and some of the other areas, is that the research moves so fast that when you get a Government commission and it is subject to obviously a budget process where they have to get money, they have to get set up, they have to hire people, that I am a little leery on whether they can move fast enough to stay up with some of the types of technology. As the doctor said earlier with Japan, we are talking 15 years but these developments could go within the next year or so, just the developments that have taken place in the last 6 months, and the chairman pointed out one area earlier today. I just am a little leery on the commission focus, only because I am looking at the bureaucracy that it will take to set it up and get it moving.

Mr. SCHEUER. Well, we never perceived this commission as being part of the problem. We have always perceived it as being part of the solution. We are trying to cure a bureaucratic problem. We are trying to cure an inertia problem, and not produce more bureaucracy and more inertia. In effect, this commission is designed to provide some leadership, to loosen the bonds of bureaucracy and overregulation and underfinance, and provide some direction and some focus and some leadership. If it can't do that, it shouldn't be born.

Mr. Kelley. Maybe we should set it outside of the beltway, then. Maybe it will be a better situation.

Mr. Scheuer. Dave?

Mr. Price. I cannot return after the vote, so I would appreciate the chance to——

Mr. Scheuer. All right, then. I am happy to yield to you then.

Mr. Price. Thank you, Mr. Chairman.

Dr. Hanna, one of the most striking aspects of your testimony is what you say about basic as opposed to applied research, and I notice in the OTA study the statements are, if anything, even stronger. Just to quote very briefly here, you talk about the option of directing Federal agencies to dedicate more of their budgets to applied and multidisciplinary research in biotechnology.

For example, you say at the NIH "support for individual, investigator-directed basic research products and projects in disciplines underlying medical biotechnology, such as cell biology, immunology, virology, neurobiology, structural biology and genetics, could be redistributed to multidisciplinary programs involving researchers from several of these disciplines." Now I'm sure you realize that in those quarters those are fighting words. I'm sure you don't include this language lightly.

I would like to know some of the findings, some of the thinking that goes into that, the rather forceful presentation of that option. I would also appreciate comments from other members of the panel who may have thoughts on this. Let me just say it is often argued that the applied research, that that is what these State efforts are going to emphasize; that if there is any place where there needs to be firm support for basic research, it has to be at the Federal level in agencies such as NIH, so it is a striking recommendation and I wonder what goes into it.

Dr. Hanna. Well, I think that that recommendation comes largely from our observation that biotechnology is uniquely multidisciplinary, and it does really require the input of several disciplines in the life sciences. I think that we are not suggesting that money be taken away from basic areas or that money be taken away from investigators that are doing work in certain areas.

Mr. Price. You do use the term "redistribution," though.

Dr. Hanna. That's right, and I think that it goes back to kind of a historic argument at NIH about whether center grants are effective ways of spending NIH money versus the individual investigator grants, and I think that we conclude that in areas such as biotechnology, which by its nature is applied—the word "technology" is in that word—that it might move applied work faster if some of the work were redistributed to multidisciplinary efforts, recognizing that that is in some circles an unpopular recommendation.

Mr. Price. I know we are running out of time. We do have a vote approaching. Any other quick comments from the panel members?

[No response.]

Mr. Price. Dr. Merrifield, do you care to venture a comment?

Mr. Scheuer. Hold on, Dr. Merrifield. I have to leave now because I can't run as fast as you can, Dave. I am going to leave, and

I am going to leave it to you to stay as long as you would like. I will be back in about 15 minutes. I have a few questions I would like to ask the panel. We have imposed upon your patience and forbearance, so if any of you have to leave, go ahead and leave and we will get our questions in by mail, but if any of you can stay for 15 minutes I would appreciate it.

Mr. PRICE. Thank you, Mr. Chairman.

Mr. MCMILLEN. Well, I think the multidisciplinary effort is almost essential in almost any area of technology now, and this is where pooling of skills and resources and risk are critically important, particularly for those areas that are beyond the individual risk capacity of individual organizations, companies.

I think that we have a mechanism for doing that, and where that exists we have been successful in putting together so many of these consortia. On the other hand, I think it is awfully important to understand that not only do we have a hangup in our culture, that we all want to be independent and do our own thing, but that is in many cases a very significant advantage in the entrepreneurial process that we put together. Where it is possible for an individual company to do something by itself, that is fine. That's where we should allow it to happen, and that's why we generate these 600,000 or 700,000 new small businesses every year. A bottom-up entrepreneurial revolution is going on in our country.

On the other hand, when a given task does exceed the capacity of individual companies, then the multidisciplinary collaborative efforts are critical, and particularly as we get now our Government laboratories and our universities and industry together in these collaborative efforts, I think we can see some spectacular results. I think that is beginning to happen almost at an exponential rate, so it is beginning to happen. I think again if we get the bears out of the way, provide risk capital, it will accelerate even further.

Mr. PRICE [acting chairman]. You are speaking, of course, mainly to the—well, your answer goes far beyond the question of what NIH priorities, for example, ought to be. You are talking about a much broader need for collaboration.

I am sorry we are so rushed. If others of you have material you would like to submit for the record, we would gladly receive that, but I too need to go vote, and so we will suspend for 15 minutes. Thank you.

[Recess.]

Mr. SCHEUER. I only have about 6 minutes because the vote just went on. Dr. Yoshikawa, could you sit down there? I have to get out of here in 6 minutes to catch this vote. This is a new roll call vote. I see that your colleagues on the panel are among the missing, so let me ask you.

First, you mentioned automobiles several times in the course of your testimony. We are quite aware that Japan and other foreign manufacturers are experimenting with new automobiles that in 5 or 10 years will get 80, 90, 100 miles per gallon. Is there any biogenetic process that could contribute to this, or is that strictly engineering?

Dr. YOSHIKAWA. It is a very difficult question to answer because I am not a scientist. Five or 10 years ago those different fields of science were totally isolated, but nowadays biotechnology, new materials, other scientific fields are converging together, so one breakthrough in one area can be utilized for many different purposes, so I am pretty sure there will be many applications of biotechnology related to findings in automobile or even computer and other industries.

Mr. SCHEUER. Can you conceive of any Government assistance, and any consortium that we could form among our domestic automobile manufacturers with some Government assistance, that could give them a 10-year goal of producing an automobile that would achieve 100 miles or 110 miles a gallon, triggering them with some of the funding for this long-term research, both cheap money and patient money, so that at the end of the pipeline they would come out with the new materials, the new systems, the new applications of electronics, computer science, and biotechnology so that we would hit the deck running and be a competitive force in global automobile production?

Dr. YOSHIKAWA. I think it is very possible. As I mentioned in my presentation, it is very important if you are going to form some committee or advisory panel to investigate that possibility, I think you should get many people from industry rather than from the policymaking circles or the universities. At least 50 percent or 70 percent of the members of the panel should be from industry, someone who is doing business for the last 5 or 10 years and someone who is going to do that business for the next 20 years, so that there can be some long-term vision.

Mr. SCHEUER. Now MITI has set up several biotechnology advisory groups.

Dr. YOSHIKAWA. Yes.

Mr. SCHEUER. Do you think these advisory groups that represent business are part of the answer to the swift progress Japan has made, typically, in these situations? Is another element perhaps some kind of a different regulatory system that Japan has as compared to ours, which enables Japanese scientists and manufacturers and Government people and researchers to make progress in a way that is less fettered and less limited by a bureaucratic regulatory process?

Dr. YOSHIKAWA. Definitely. Well, in Japan most companies doing biotechnology research are large, well-established companies—chemical companies, pharmaceutical companies. Those presidents and chairmen then probably knew each other for the last 25 or 30 years, probably went to the same school. Probably their wives know each other. Probably their children went to the same school. As well-established executives, they can come up with a consensus much easier than their American counterparts.

Mr. SCHEUER. This is the Japanese version of the "old boy club"?

Dr. YOSHIKAWA. Yes, but those old executives from Fujitsu, Takeda, Suntory, they get together and think about what is important for Japan in 10 or 15 years, and I am pretty sure they realize what is important for Japan before what is important for their own companies, and come up with national, long-term strategies. That kind of a vision for the national interest is very important, so for this purpose I think you should get many people from industry who have been doing business the last 10 or 15 years and who are going to do business the next 20 years. That is important.

Mr. **Scheuer**. I ask unanimous consent that we be able to submit questions to you in writing, Dr. Yoshikawa. You gave us some marvelous testimony and we do want to follow up.

There being no objection, so ordered, and we will be in touch with you. Thank you very much. I have to run to get this roll call vote, so this panel is excused, and when we come back Doug Walgren will Chair the next panel.

[Recess taken.]

Mr. **Walgren** [acting chairman]. Well, let me start us up again and call the second panel: Dr. Robert Cook-Deegan, the senior associate for the Office of Technology Assessment; Dr. Ruth Kirschstein, director of the Institute of General Medical Studies, with NIH; and David Nelson, executive director of the Office of Energy Research with DOE.

Welcome to our process, folks. We appreciate your patience. As I am sure has been said before, the written statements will be made part of the record and you can feel free to focus on parts of a written statement or underscore it in whatever way you would like to, to set out the points that you would like to have leap out of the verbal testimony for those who work with those records.

So with that, why don't we go through in the order that I have introduced you to the record, and we would be pleased to hear you, Dr. Cook-Deegan.

STATEMENT OF DR. ROBERT COOK-DEEGAN, SENIOR ASSOCIATE, OFFICE OF TECHNOLOGY ASSESSMENT

Dr. **Cook-Deegan**. Thank you, Mr. Chairman. My name is Bob Cook-Deegan, and I directed the OTA report that was released on April 27th of this year. I know you were at the hearing where that report was released, so I won't go into the details of what the definitions of genome projects are. What I was asked to do by the committee was to focus on issues of coordination, specifically interagency coordination, and I will do that.

Before I do that, though, let me say two things about genome projects that I think are distinguishing characteristics. First of all, we are talking about a program to establish new technologies and new methods to do things; and second of all, probably the main thrust of genome projects is going to be to create research resources that are collective. What that suggests—incidentally, the purpose of that is essentially to create tools for further research and for commercial exploitation—the bottom line of that introductory remark is that the whole idea behind genome projects is that they are a collective effort, and I will come back to why that is important in a moment.

In dealing with issues of coordination, I think there are four levels of coordination that have different mechanisms associated with them, and let me go through them very quickly. (1) Among nations there has to be international collaboration, (2) between agencies of the U.S. Government and other American funders, such as the Howard Hughes Medical Institute, (3) within agencies there has to be coordination, and then (4) among scientists who are actually conducting the work.

I am not going to talk about coordination within agencies or among scientists because I think those mechanisms are in place and they work quite well. Those mechanisms are not completely elaborated yet, but people are working very hard on that. I will focus most of my remarks on interagency coordination, but first I want to say a couple of things about international cooperation.

First, immediately after that April 27th hearing, a new organization was formed—about 3 days later—up in Cold Spring Harbor, called the Human Genome Organization. Victor McKusick of Johns Hopkins University is the chairman—I guess he is called president—of that new organization. The Human Genome Organization, or HUGO, was created specifically for the purpose of international scientific collaboration on genome projects. It is currently being formed and it will meet for the first time, I think, on the 8th and 9th of September in Geneva, Switzerland.

There is another international meeting that will actually follow that one. It will take place in Valencia, Spain in October, where whatever isn't resolved at the HUGO meeting would presumably come to that meeting. There will be members of various agencies from the U.N. and from European governments at that Valencia meeting, so I think some structure for international collaboration is going to be put together in the next 3 or 4 months.

In the United States, there are four principal players in genome projects. There is the National Institutes of Health, the Department of Energy, the National Science Foundation, and the Howard Hughes Medical Institute. I will go into some details about them, but before I do that I wanted to say what I think are the strengths and the weaknesses of the current coordination mechanisms.

First and most importantly, I think that to date the lack of a coordination mechanism hasn't made much difference. The projects have gone ahead. Money is being spent. Good projects are being supported, and I don't think it has been a problem to date in support of genome projects.

I will say, however, that I think there are problems that can be foreseen in coming years if more elaborate mechanisms aren't put into place. I base this judgment on the fact that I think there are different notions, certainly among scientists and administrators on kind of the trench level within agencies, about what the long-term vision of genome projects is and what should be accomplished by the projects, and I think a mechanism needs to be put into place to harmonize those visions.

I will start my remarks about formal coordination by noting that the National Research Council report urged that there be a lead agency designated to head up the efforts, and I want to focus on three notions of what a lead agency might be. You could take that recommendation many ways.

One, you could say this means that NIH or DOE or NSF should do all the work, and the work at other agencies should be stopped. I don't think that is rational, and I doubt that that is what the committee meant. There is really no argument in favor of that, I don't think.

Perhaps, and I think this is probably what the committee meant when they made that recommendation, it is that eventually the bulk of funding and support would all go through one agency, and therefore interagency cooperation wouldn't be that big of a deal because there would already be planning in place by virtue of the fact that almost all the work was being done in one place. I think that might be a good long-term strategy, but it is certainly not the case right now.

For the fiscal year 1989, which is the one that is in the budget cycle right now, the NIH has requested $28 million and the Department of Energy has requested $18 million, so there is enough of a substantial minority outside of the NIH that I think it would be difficult to imagine that you could call one of those (NIH or DOE) the lead agency or something like that, although I would say that in the long run perhaps it will evolve that way. As things become more specialized, perhaps genome projects won't be seen as a conglomerate whole but rather will be subdivided into more specific technological areas.

There is one coordination mechanism that is already in place, and that is a subcommittee of the Committee on Life Sciences in the Office of Science and Technology Policy. This involves NIH, NSF, the Department of Energy, and also the Howard Hughes Medical Institute, so it does involve the four principal players. That subcommittee has been meeting quite frequently and they have been exchanging a lot of information, and I want to say a couple of words. I think, for one thing, it is a good step in the right direction to have formed that committee, but I think that it is not going to do the job that needs to be done. I don't think that communication among the agencies has ever been the crucial problem.

I think, instead, the crucial problem is this differing vision of what genome projects mean, and I don't think an organization within the OSTP or that close to the political centers of power is going to be able to harmonize those visions, in part because it is so close to the ideological centers of power, and also because I think it is difficult for purely Government agencies or interagency groups to come up with a coherent vision.

I think most of the very difficult questions that need to be addressed about genome projects have a lot of scientific content to them. You need to make decisions about which data bases to establish, which repositories to support, and what long-term strategy to pursue, and I think that a lot of outside scientific advice needs to be sought in that process.

Having said that, what are the options for the committee to take action on? One is to take no action, say things are actually going pretty well and we shouldn't fix the problem until it is worse, and I think that is a rational policy.

The second possibility is to encourage the agencies to, among themselves, solve the problem. That would be something in the form of a memorandum of understanding where there was an agreement on how the agencies would cooperate in the future. For example, at the last hearing Dr. Wyngaarden suggested that the advisory committees might share overlapping members.

I think that is one strategy that could be followed, but I don't think that particular suggestion would work, because we have seen overlapping membership on the DOE committee, the OTA committee, the National Research Council committee, and the Howard Hughes Medical Institute advisory committees. All four of those groups have written reports that reach largely coherent but in detail incompatible recommendations, and yet there has been overlapping membership in those existing committees, so I think that that problem is going to persist until there is some place to articulate a common vision.

Now what are the choices for doing that? One would be to designate an existing outside scientific group to do that, for example, the Human Genome Organization, this newly forming organization. That would have the advantages of kind of pulling together international and national planning, and it means the people with the expertise who have already organized themselves would be able to provide a common source of advice to all the agencies, and all that would really be needed then would be for the agencies to agree to pay attention to what the Human Genome Organization has to say.

Another possibility would be to ask the National Academy of Sciences to play a role, either by appointing a committee or by becoming part of the advisory network. A third possibility is for the agencies themselves to directly appoint a joint advisory committee that they would agree to share. I think all those are possibilities. They could be established within NIH or they could be established autonomously. However, I think that really is an open question. I think there are a lot of acceptable solutions.

That brings me to a final course of action, however, and that is legislation. In S. 1966 there is a provision that would call for a Human Genome Advisory Committee that includes industry, that includes outside scientists and the principal three Federal agencies. I think that that bill is an improvement over current policy, and I think that the committee could be encouraged to go ahead and follow that course of action.

I think one no-lose strategy would be to fully intend to incorporate those provisions into the bill in the long term, but leave open the opportunity for the agencies, between now and whatever time a House-Senate conference is called on this bill—assuming that it passes the House, there would presumably be a conference—I think it would be a good thing to give the agencies up until that point of the House-Senate conference to come up with some agreement of their own. If they can't agree, then you pass the bill. If they can agree, then the policy you would put in place is better than the current policy.

Thank you.

[The prepared statement of Dr. Cook-Deegan follows:]

TESTIMONY OF ROBERT MULLAN COOK-DEEGAN, M.D.
SENIOR ASSOCIATE, OFFICE OF TECHNOLOGY ASSESSMENT
BEFORE THE SUBCOMMITTEE ON NATURAL RESOURCES,
AGRICULTURE RESEARCH, AND ENVIRONMENT
AND THE SUBCOMMITTEE ON SCIENCE, RESEARCH, AND TECHNOLOGY OF THE
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
U. S. HOUSE OF REPRESENTATIVES

July 14, 1988

COORDINATION OF GENOME PROJECTS

My name is Robert Cook-Deegan. I am a Senior Associate at the Office of Technology Assessment (OTA), and directed the OTA assessment, Mapping Our Genes – Genome Projects: How Big? How Fast?. That report was released at a hearing of the Energy and Commerce Subcommittee on Oversight and Investigations on April 27. The OTA report discussed coordination of genome projects, and the topic was prominent in remarks at the April hearing. This hearing, two and one-half months later, provides an opportunity to assess progress and articulate more specific options for action by Congress. I will describe the problem, summarize existing mechanisms, and offer three specific options for action by this committee.

Genome projects are described in several reports by the National Research Council (NRC), the Howard Hughes Medical Institute (HHMI), a Department of Energy (DOE) Advisory Committee, and OTA. While these reports differ in many details, all agree on the importance of some coordination of effort and the need for planning so that the collective efforts of many molecular genetics laboratories can be integrated into a set of useful research resources. Various types of chromosomal maps, DNA stock centers, genetic databases, and other common resources will be among the principal results of genome projects. Each of these must include data or materials from many groups to be useful, and this will require foresight and cooperation.

Four levels of coordination

Coordination must occur at several levels: among nations, among U.S. organizations, within those organizations, and among scientists. Each of these four levels has its own appropriate mechanisms for coordination. There are mechanisms already in place to coordinate grant programs, databases, and research infrastructure within the National Institutes of Health (NIH), DOE, the National Science Foundation (NSF), and other agencies. This is not to say the details have been worked out — they certainly have not — but agencies are hard at work and legislation is unlikely to help. Communication among investigators in hundreds of laboratories can best be left to the normal scientific channels, which work remarkably well. I will therefore focus on the top two levels: coordination across national borders and among agencies in the United States.

Since the April hearing, several foreign governments have expressed increasing interest in genome projects. The French have allocated special funding for genome work, and there are moves afoot to make genome projects a centerpiece for biotechnology within the European Economic Community. Scientists in the Federal Republic of Germany, the Netherlands, Spain, France, and other countries are reportedly enthusiastic. There is less governmental support in the United Kingdom, but privately funded projects are already underway there. Finally, genome projects in one form or another may become part of the Japanese proposal for a Human Frontier Science Program (HFSP). Japanese scientific and technical projects for DNA sequencing technologies, mapping of human chromosome 21, and other projects are proceeding despite uncertainty about the HFSP.

A new organization, the Human Genome Organization (HUGO), has been created to respond to the need for additional scientific coordination. This group was formed at a scientific meeting at Cold Spring Harbor Laboratories in late April. HUGO is now being organized by Victor McKusick of The Johns Hopkins University. HHMI is supporting the first meeting of the HUGO council in late September, to be convened in Geneva, Switzerland. Tentative plans for HUGO would provide for offices in North America, Europe, and Asia. HUGO has the potential to meet most of the needs for overall international coordination. An international meeting in late October will take place in Valencia, Spain to debate whether further steps are needed. That meeting will include representatives from the United Nations, foreign science ministries, and international scientific organizations. I will come back to a possible way to unify international and interagency planning near the end of my statement. Specific issues will undoubtedly require more formal international collaboration, such as international materials repositories and databases. A good model is the collaboration among those operating DNA sequence databases; an international committee and formal coordination agreement exist among GenBank (in the USA), the European Molecular Biology Laboratory (in Europe), and the DNA Database of Japan (in Asia) to collect and distribute data.

Coordination of genome projects in the United States will involve at least the four principal organizations conducting relevant research. NIH, DOE, and NSF are federal agencies, and HHMI is a private medical institute. For projects dedicated to genome work, DOE has requested $18 million for 1989; NIH has requested $28 million. If one includes related molecular genetics and support of relevant infrastructure, however, NIH is overwhelmingly dominant, funding over $400 million in projects, compared to tens of millions for DOE, NSF, and HHMI. (NIH has by far the largest biomedical research budget among these, over $6 billion for 1988. DOE, NSF, and HHMI each funded $200 to $250 million of life sciences research. The relative contributions of these funding sources may change in future years, depending on decisions of appropriations committees, future administrations, and the HHMI board of trustees.)

In its report, the NRC committee urged that a lead agency direct genome projects. If this means that one agency does most of the work and others do less, then there is no disagreement but it is already policy. If it means termination of efforts at NSF and DOE, then OTA does not concur. If it means that one agency should command most of the resources so that formal interagency planning is not necessary, this may be a good long-term goal, but it will take several years to evolve. In the meantime, there needs to be a mechanism for coordination. In the near future, NIH will likely support most genome work – that most closely related to its current projects – with NSF, DOE, and HHMI continuing to support work within their mandates. NIH would presumably provide most funding for mapping complex genomes, improving detection of DNA, cloning DNA, studying particular genes, small scale sequencing, and maintaining databases and repositories, but other agencies would make substantial contributions. DOE and NSF will likely support scientists devising new analytical instrument~~al~~s, automating DNA analysis, and improving computer analysis of genetic data. DOE may well take the lead when gene mapping or regional DNA sequencing become more akin to production work awaiting completion than pursuit of pure science.

The current status of interagency coordination is excellent at the level of day-to-day work, with pooling of resources, joint planning of workshops, coordinated support of databases, and frequent communication among agency personnel. There are two problems at present, however. First is that those in the different funding organizations have distinct and incompatible visions of what genome projects are and, more markedly, what they will become.

Different visions lead to different long-term strategies. The Office of Science and Technology Policy (OSTP) has established a genome subcommittee of its Committee on Life Sciences that includes representatives from NSF, DOE, NIH, and HHMI (as well as the Office of Management and Budget). This subcommittee has met frequently, and has exchanged information, but communication among administrators has never been the bottleneck. The larger problem has been differing visions of the future. Could the OSTP subcommittee harmonize these visions? I think not. It seems unlikely that administrators from the four funding agencies could articulate a common agenda, without the direct involvement of scientists directly familiar with relevant research. The pivotal decisions involve arcane technical and scientific issues, such as what kinds of maps need to be constructed and what types of databases or material stock centers to establish.

The second problem is the closeness of information exchange to the centers of political power. There is a natural tendency for those representing agencies to put the best light on current efforts when discussions are taking place near the White House. Frank discussion of problems among agencies is unlikely to take place when OMB and OSTP are directly involved.

It seems to me that the critical missing element is a source of high level scientific advice shared by all the agencies, but distinct from them. We do not need scientists to tell government agencies how to spend their monies — that would be inappropriate. We do need a group that can help articulate a common set of goals, and strategies for achieving them. This would involve the groups already working with OSTP, but would add outside experts. Agencies could then use existing planning mechanisms and advisory bodies for tactical planning, to guide their respective efforts. This would benefit not only U.S. agencies, but also those planning foreign efforts. There are several different options for forming an outside scientific advisory group.

Options for Interagency Coordination

Your committee might follow any of three courses: take no action, encourage agencies to sign an interagency memorandum of understanding, and establish an advisory committee by legislation, along the lines of the genome board in S. 1966. I believe a combination of the second and third options is optimal.

Take no action. NIH, DOE, NSF, HHMI, and foreign governments could continue to plan independently. This would preserve the healthy pluralism that characterizes American science. It would, however, greatly complicate reaching consensus in the long run. A new means of coordinating work must be newly confronted every time a widely useful database, stock center, mapping effort, or technology is produced. Funding and support arrangements have to be forged for every effort that crosses agency or international boundaries. Many projects would not cross such boundaries, and could best be solved by one agency alone. But these are not the troublesome cases, and existence of a coordination group should not impede their solution. The collective nature of mapping and technology development efforts will undoubtedly produce many programs that do cross boundaries, probably enough to justify a formal coordination mechanism to identify and plan for them.

The agencies could go one step towards coordination by ensuring some overlap of members among existing groups advising NIH and DOE. This was suggested by Dr. Wyngaarden at the April 27 meeting. I am not confident that this would solve the problem. My pessimism is based on the experience of genome planning to date. There have been separate advisory groups convened by DOE, NRC, HHMI, and OTA. In all cases, there has been overlap of at least two members, yet the recommendations are incompatible in many respects. Most of the disagreements are insignificant, but some inconsistencies do make planning difficult (for example, whether there should be one database management center or several). Given the inability of overlapping representation to prevent such incompabibility in the past, I see no reason to believe it would do better in the future.

Interagency Memorandum of Understanding. This would entail agreement among the principal funding organizations (including HHMI) on a process for formulating goals, rationally planning research programs, facilitating communication, and supporting research infrastructure. Agreement on a process to appoint an outside advisory body is an essential component. NIH, DOE, NSF, and HHMI could, for example, ask HUGO to appoint a subgroup of its council, perhaps its U.S. council members, to serve as an advisory body to all the agencies, and to track activities in all of the agencies. HUGO would know what was happening both nationally and internationally, which would improve both national and international planning. HUGO is likely to prove central in planning scientific symposia and data exchange arrangements in any event, and so formally involving it would be only a slight change. Alternatively, the agencies could ask the National Academy of Sciences to appoint an advisory group, or could jointly appoint an advisory committee (which could be autonomous or housed in NIH). The agencies would agree to respond to recommendations of the advisory board within a specified period. For any of the options, costs for meetings and staff functions could be proportionately funded by the principal four agencies. There will have to be three or four staff, at least initially, to arrange meetings, monitor developments, and write reports. Staff and planning activities could expand or contract in future years, in response to need.

Legislation establishing a strategic planning board. This is the option embodied in S. 1966. The human genome provisions of that bill would improve current coordination. I believe it should be implemented if agencies do not agree on a better mechanism. The bill includes the appropriate agencies, and ensures that advice from scientists, industrial experts, and others will be heard. The agencies might, however, be able to devise a mechanism they all agree is better. It can be argued that they should be given the opportunity to do so. If they cannot agree among themselves, then it will fall to Congress to solve the problem.

One practical course of action would be for this and other committees to retain the human genome section of S. 1966, fully intending to implement it. If agencies fail to sign an interagency agreement by the time of the House-Senate conference, then the bill could be passed as is, or amended to provide alternative means to the same end. An interagency agreement would include a process for selecting an outside advisory group, a list of functions for it, and a timetable for establishing it. Of course, having an agreement does not mean that it will be effective. The same point can be made about legislation, although legislation would have better prospects for enforcement.

The human genome advisory panel in S. 1966 signals Congress's judgment that interagency coordination is needed. If agencies sign an agreement in the next several months, however, the human genome provisions could be struck from the bill in conference, signalling Congress's satisfaction that agencies have put their houses in order.

Mr. WALGREN. Thank you very much. We appreciate that testimony, and now we will turn to Dr. Kirschstein.

STATEMENT OF DR. RUTH L. KIRSCHSTEIN, DIRECTOR, INSTITUTE OF GENERAL MEDICAL SCIENCES, NATIONAL INSTITUTES OF HEALTH

Dr. KIRSCHSTEIN. Thank you. I would like to express my appreciation for the opportunity to present the activities of the NIH and put them in perspective as they relate to the research performed and supported by the NIH over the past 20 to 30 years.

In the 1984 publication from the Office of Technology Assessment on commercial biotechnology, it was determined that there were three key factors—government funding of basic and applied research; adequate numbers of trained personnel, and the availability of funds for industrial development—which would influence a country's competitive position in world markets, but of all of these, the support of basic research was considered to be particularly critical.

Based on that, in 1985 the NIH had its Advisory Committee to the Director discuss the role of fostering the Nation's leadership in biotechnology, and I think it is fair to say that the current health of the biotechnology enterprise and the competitive advantage that you have been hearing about this morning that NIH holds—that the United States holds—is in large part due to the substantial involvement of NIH in the support of basic research. In fact, at the request of the Senate Committee on Appropriations NIH this year prepared and submitted a report related to its role in biotechnology research, and I would like to submit that report to this committee for the record.

Mr. WALGREN. Without objection, we will take it.

Dr. KIRSCHSTEIN. In fiscal year 1987 the total Federal support, as you heard earlier today, was approximately $2.7 billion, and over 85 percent of those funds, namely $2.4 billion, was provided by NIH.

Furthermore, as you know, this investment of NIH has now allowed scientists to develop the new technologies that Dr. Cook-Deegan was just talking about, to be able to plan for the characterizing of the human genome and the genomes of many other complex organisms. I think it is very clear that the information about the entire genomic material of man is going to have profound implications for understanding, diagnosing, preventing, and treating more than 3,500 human inherited diseases as well as many other diseases, and also it will help us to learn, as Mr. Scheuer was asking previous witnesses, more about the factors in our environment that cause certain diseases and how we may be able to prevent the deleterious effects.

Now over the years NIH has, as we have said, provided a great deal of money to study complex genomes in general. In 1987 it was actually over $365 million, and of that, $110 million was specifically focused on human disease. However, in fiscal year 1988 Congress provided $17.2 million in new monies to NIH for what is basically a new program, a program dedicated to systematically mapping and sequencing the entire genomic material. This was recommended by the OTA report and by the report of the National Research Council.

The information that is going to come out of that project will be so massive that the scientific community will be facing a serious administrative challenge, and this is a challenge that encompasses not just the genomic data but a large and growing collection of related computer data bases as well. We feel that this coordination of the major information services will be the unique role of the NIH's National Library of Medicine through the National Biotechnology Information Center, which can work and will work with all the Federal agencies which support molecular research in the life sciences, in order to build bridges between key data bases and computer systems for supporting and sharing this information, and this is absolutely necessary for optimal progress in biotechnology.

Furthermore, in recognition of the high priority that NIH gives to mapping and sequencing the human genome, a new office has been established within the Office of the Director of NIH, an Office of Human Genome Research, and it will be headed by a new Associate Director. The function of that office will be to provide coordination, integration, review of progress, and planning of the analyses needed from the data that are put together.

But if we are going to assume that further biotechnological advances can occur, as well as progress in mapping and sequencing the human genome, we have to face the fact that there is a need for expansion of research training efforts in biotechnology. The OTA recognized this in its report, and indeed in March of 1988 NIH put together an expert panel of scientists who attended a workshop which we entitled "Biotechnology Research and Research Training". All of the Federal agencies that were involved in this, including the Department of Agriculture, the National Science Foundation, the Department of Energy, all attended this meeting, as well as large numbers of people from both the industry, State governments who are involved in biotechnology, and the universities.

It was the consensus of the group that the enormous growth of the biotechnology industry has led to serious shortages of scientific personnel in academia and in industry, and that there is a great and critical need to provide such research training for a generation of scientists with multidisciplinary, interdisciplinary backgrounds in fields of biophysics, theoretical mathematics, physical chemistry, molecular biology, and chemical engineering. The conclusions of that meeting were also included in an April, 1988 report to the Senate Appropriations Committee entitled, "Biotechnology Research and Research Training", and I would like to provide that to this committee as well.

As you have been hearing all today, there is a great need for collaborative and coordinated efforts between Federal agencies. I want to assure you that even without any formal mechanism, this coordination is very strong, and indeed stronger links are being forged every day. The activities of NIH, DOE, and the National Science Foundation are complementary to each other.

At the working level, the scientists in the laboratories either work directly together or collaborate. For example, NIH supports many researchers in the DOE National Laboratories, contributing

$26 million in fiscal year 1986 to the biotechnological projects handled there. You heard earlier today about the MIT Bioprocessing Engineering Center. That center is supported primarily by the National Science Foundation, but the National Institutes of Health for the last several years has contributed funds to that center in coordination with NSF, particularly for the training of biotechnological personnel such as I mentioned.

To make sure that the genome projects are coordinated, a professional staff member from my own institute served a 6-month detail at DOE to provide technical assistance in the peer review of the projects that DOE was doing in the genome effort. Another member of my staff, a professional member, serves as the NIH-designated liaison to the Agriculture Department on biotechnology. Indeed, that individual is a special assistant to me in biotechnology, because I feel that this area is so important that we have so designated this person.

The Department of Energy and we are talking about more formal interagency coordination. We are planning this common membership from subcommittees on the advisory board, and we plan other areas where we can coordinate through workshops and careful planning how we will do the genome projects. In addition, all scientific endeavors by their very nature are international in scope, and from the very beginning of all these research efforts scientists from Europe, Canada, and Japan have been collaborating with U.S. investigators.

It should be said that through NIH support, the products of basic molecular genetic research have enabled biotechnology firms to produce large quantities of, for example, human growth hormone, human insulin, tissue plasminogen activator to treat heart attacks, Factor 8 to treat one form of hemophilia—that is the subject of the article in the Wall Street Journal this morning—

Mr. WALGREN. I am sorry to interrupt, but let me give you one minute to summarize, and I feel I ought to keep this hearing really on track so we don't go deep into the afternoon.

Dr. KIRSCHSTEIN. I do want to say one thing about the fact that NIH intramural scientists are deeply involved in collaborating with small industries, and in therefore implementing the Federal Technology Transfer Act. We expect that NIH will play a greater and more critical role in support of both basic research and other aspects of enhancing commercial applications, and we are committed to coordination, both interagency, intra-agency, and at the international level.

[The prepared statement of Dr. Kirschstein plus the report mentioned above follows:]

Statement of Ruth L. Kirschstein, M.D.
Director, National Institute of General Medical Sciences
National Institutes of Health
before the
House Committee on Science, Space and Technology, Subcommittees on
Natural Resources, Agriculture Research and Environment
and Science, Research and Technology

Mr. Chairman, Members of the Subcommittee,

I would like to thank you for the opportunity to present the activities of the National Institutes of Health (NIH) in Biotechnology and to put in perspective the relationship of this most important new aspect of biological science and commercial enterprise to the research performed and supported by NIH for the past 20-30 years.

Before I begin my testimony, I would like to share the Administration's views on H.R. 4502 and S. 1966. I would like to stress the Administration's support for the intent of this legislation--that is, the goals of promoting research on biotechnology and enhancing the competitiveness in biotechnology of this country. However, the Administration opposes the enactment of these bills because they duplicate current activities and would most likely impede, rather than improve, our competitiveness in biotechnology. The addition of more layers of bureaucracy and the other requirements proposed by the bills are not only unnecessary but they are costly and will not improve our country's position with regard to competing with other nations.

In its 1984 report on commercial biotechnology, the Office of Technology Assessment (OTA) determined that three key factors--government funding of basic and applied science, adequate numbers of trained personnel, and availability of funds for industrial development--influence a country's competitive position in world markets. Support of basic research, in particular, was considered to be critical in maintaining the science base upon which this technology rests and in stimulating further advances and commercial development.

In 1985, the NIH Director's Advisory Committee discussed the role of NIH in fostering the Nation's leadership in biotechnology. The current health of the biotechnology enterprise and the competitive advantage that the United States now holds, is, in large part, due to the substantial investment in basic research, particularly in molecular biology, over the past several decades, through the efforts of NIH.

At the request of the Senate Committee on Appropriations, the NIH, this year, prepared and submitted a report related to its role in both the support and application of biotechnology research and I would like to submit that report to this Committee. It documents, in detail, the commitment of NIH to this endeavor and the contributions made by NIH scientists to advancements and commercial applications in this area. In Fiscal Year 1987, total Federal support for biotechnology research and development was approximately $2.8 billion. Over 85 percent of these funds ($2.4 billion) were provided by the National Institutes of Health.

As you know, the investment of the National Institutes of Health in fundamental research in genetics and molecular biology over this past 20-30 years has led to new technologies for cloning and analyzing DNA, the genetic material of all living organisms. These discoveries have enabled scientists to develop a new initiative, that of characterizing the human genome and the genomes of a number of other complex organisms, which serve as model systems. Information about the entire genetic material of man will have profound implications for understanding, diagnosing, preventing, and treating the more than 3,500 human inherited diseases, and also will enhance our understanding of the normal biological processes by which we maintain our health, and our children develop into healthy adults. In addition, this initiative will help us learn more about how factors in our environment cause certain diseases and how we may prevent these deleterious effects.

In Fiscal Year 1987, NIH provided over $365 million to support about 3,000 research projects devoted to the elucidation of complex genomes. Of this, about $110.5 million was specifically focused on studies of human disease. Scientists supported by NIH are now engaged in many projects to "map" or pinpoint the specific location on the human chromosomes of those genes reponsible for inherited disorders. Researchers have already mapped, and thus found, the approximate locations of the genes for Huntington's disease, Duchenne muscular dystrophy, retinoblastoma (cancer of the eye in children), some forms of manic-depressive illness, cystic fibrosis, cancer of the colon, color blindness, and Alzheimer's disease, to name but a few.

While these human genes have already been mapped to their respective chromosomes, they ~~represent~~ a minute fraction of the total genetic material. At a meeting of the Advisory Committee to the Director, NIH, held in October 1986, the crucial role of the NIH in mapping and sequencing was emphasized. There was a consensus that a phased approach was needed to develop complete information, not only about the human genome, but about the genomes of many other organisms as well. The first phase would be to develop mapping strategies and to map the entire genome. Sequencing projects should come later, although the development of improved sequencing techniques should be supported now.

In Fiscal Year 1988, $17.2 million in new monies was provided to NIH for a program to develop new technologies, improve existing technologies, and increase analytical precision in order to implement, in a systematic way, the mapping and sequencing of the entire genomic material, as recommended in both a report from the National Academy of Sciences (NAS) and the one from the Office of Technology Assessment (OTA). The President's budget request for FY 1989 increases the funds for NIH for the "genome project" to $28 million.

The information to be gained from mapping and sequencing complex genomes is so massive that the scientific community and the builders of information systems face a serious administrative challenge. This challenge encompasses not just genomic data but a large and growing collection of related computer databases as well, which encode new knowledge about other important molecules, and about cells and tissues. Among these are the Hybridoma Data Bank, the ATCC Cell/Tumor Bank, the Human Mutant Cell Repository, the Human DNA Probe Repository, the Human Gene Library, the Protein Information Resource, and GenBank, as well as the European Molecular Biology Laboratory (EMBL) Bank of Nucleic Acid Sequences and the DNA Databank of Japan.

All of these databases have been referred to as an electronic "Tower of Babel." They often use different words to describe the same thing, as well as different computer file designs and different methods of searching and retrieving information, making it difficult for a scientist to learn how to use more than one or two of them.

The coordination of these major information services will be the unique role of the National Biotechnology Information Center of the National Library of Medicine. The Center will work with all the Federal agencies which support molecular research in the life sciences to build bridges between key databases and computer systems for the sharing of information. It will develop standards, both in human language and computer language, for linkages among databanks.

The contents of these databases will become available through the Center via a common digital language and a series of computer networks. In addition, the Center will sponsor, via grants and contracts to academic institutions, commercial establishments and other parts of the private sector, research related to new methods of information representation, storage, and retrieval.

These vital information-handling services are absolutely necessary for optimal progress in biotechnology.

In recognition of the high priority that NIH gives to the mapping and sequencing of the human genome and the overarching planning and resource demands of a systematic targeted effort, a new Office of Human Genome Research has been established within the Office of the Director, NIH, and will be headed by a new Associate Director. The function of the Office will be to provide coordination, integration, review of progress, and planning in genomic analysis research. A particular focus will be the development of new proposals to maximize the efficiency of information exchange regarding new mapping data, improve techniques for storage and handling of biological materials, and enhance data processing and analysis. Research goals and long-range plans will be formulated with the guidance of an NIH Program Advisory Committee on the Human Genome and an internal NIH Working Group on the Human Genome. This strategy will allow centralized coordination of a trans-NIH effort while maintaining the elements of peer review and program planning that are essential to a successful research initiative.

I would again emphasize that this genome project is only possible because of the biotechnological advances that have been made over the years. To assure further biotechnological advances, as well as progress in mapping and sequencing genomes, there is a need for expansion of research training efforts in biotechnology. This has been recognized by many persons, including both a group of advisors to the OTA and an expert panel of scientists who, in March 1988, attended an NIH-sponsored workshop on "Biotechnology Research and Research Training." Participating in this workshop were representatives of state-sponsored biotechnology organizations, university biotechnology programs, and a number of Federal agencies, including the Department of Agriculture, the

Department of Energy, and the National Science Foundation. The major topic of discussion was the need for increased manpower by both the academic and industrial sectors in their respective biotechnology endeavors. It was the consensus that the enormous growth of the biotechnology industry has led to shortages of scientific personnel in academia and in industry. Indeed, in order to undergird future advances in biotechnology, there is a critical need to provide research training for the next generation of scientists. Individuals with an increasingly broad range of skills are needed, as well as individuals with an interdisciplinary background ranging across biophysics, theoretical mathematics, physical chemistry, molecular biology, computer science, and chemical engineering. The conclusions from this meeting were included in an April 1988 report to the Senate Appropriations Committee entitled, "Biotechnology Research and Research Training," which I would like to submit to this Committee as well.

Mr. Chairman, as your proposed legislation recognizes, there is a great need for collaborative and coordinated efforts between Federal agencies, industry and academia. I want to assure you that, even without formal legislation, such coordination is already very strong, and indeed, as new advances occur in related technologies and in gene mapping and sequencing projects, we are all forging stronger links. As the OTA report states, the activities of NIH, DOE, and NSF are complementary to each other.

At the working level, scientists funded by all three agencies are either directly doing research together or are collaborators. For example:

- NIH supports many researchers in the DOE National Laboratories. In Fiscal Year 1986, a total of $26 million of research grants was awarded to DOE, much of it for biotechnological projects.

- Support for GenBank, the nucleic acid sequence data bank, established by NIH in 1982, has come from all three agencies and, while responsibility for the oversight of this contract is with NIH, workers at the DOE Los Alamos National Laboratory are doing the actual collecting, analysis and entry of the sequences into the database.
- NIH is cooperating with NSF in the support of the Biotechnology Process Engineering Center at MIT, which is training chemical engineers and biologists in areas of molecular genetics, bioprocess engineering, protein engineering, and cell culture and hybridoma technologies.
- The meeting sponsored by NIH on research training in biotechnology, as well as a number of workshops on gene mapping and sequencing, have involved the active participation of DOE and NSF staff in their planning, in presentations and in discussions during the sessions. A member of the professional staff of my Institute, NIGMS, served a six-month detail at the DOE to provide technical assistance in the review of proposals related to the genome project. The staffs of all three agencies, along with persons from the Howard Hughes Medical Institute are currently planning a series of workshops including one on the social, ethical and economic issues which may arise as a result of a great increase in detailed knowledge related to the genetic make-up of human beings.
- A member of the professional staff of my Institute serves as the NIH designated liaison to the Agriculture Biotechnology Research Advisory Committee of the Department of Agriculture which advises the Secretary of that Department on matters concerning agricultural biotechnology research and the attendant regulations for the conduct of this research.

Furthermore, discussions have already taken place with the Department of Energy concerning the need for more formal interagency coordination. It is understood that each agency must have its own agenda, based on its mission and historic involvement in genetics research. However, it is also recognized that there will be many more opportunities for collaborative efforts. These opportunities can be identified and initiated through shared membership on an advisory board. Such a mechanism will facilitate the already ongoing interagency coordination that is essential to maintain the momentum in this exciting and critical area of biotechnology and in the genome project.

In addition, Mr. Chairman, scientific endeavors, by their very nature, are international in scope. From the very beginnings of the research efforts scientists from Europe, Canada and Japan have been collaborating with U.S. investigators. The efforts regarding the collection and management of the information in the nucleic acid sequence databanks are shared by the scientists of the U.S. GenBank, the European Molecular Biology Laboratory, and the DNA Databank of Japan. Coordination of these efforts is achieved by an informal governing board of senior scientists from all three groups. This board meets once a year and, in the interim period, the scientists actually handling the data communicate regularly through computer networks and by visiting each other's facilities. Such an informal meeting of scientists occurred in Heidelberg last week, whereas the previous one was held in Washington in November. In regard to the genome project, also, international collaborations are well established and a new international Human Genome Organization is being formed.

We are, of course, aware that the Biotechnology Competitiveness Act of 1987 has passed the Senate, creating a National Biotechnology Policy Board and that your proposed legislation, the Biotechnology Science Coordination and

Competitiveness Act of 1988 (H.R. 4502) would establish a national advisory commission to promote and coordinate scientific information and research on biotechnology. What I would like to reemphasize is that the National Institutes of Health is already promoting and coordinating such endeavors and that our efforts have been most successful. For example:

- ° Through NIH support, the products of basic molecular genetic research have enabled biotechnology firms to produce large quantities of human growth hormone, human insulin, tissue plasminogen activator to treat heart attacks, Factor VIII to treat one form of hemophilia, an improved vaccine to prevent hepatitis, alpha-interferon for the treatment of a form of leukemia, as well as diagnostic kits for detection of AIDS antibodies, for several genetic diseases, and for some viral and bacterial infections.

Clearly, we agree that the further enhancement of biotechnology transfer must be facilitated. NIH has instituted a number of policies to promote such transfer:

- ° Through its Small Business Innovation Research (SBIR) Program, NIH supports the private sector in its research and development activities and aids in the commercialization of innovations, many of which are derived from federally supported research. As required by law, in Fiscal Year 1987, NIH set aside $61 million for the SBIR Program. A considerable fraction of the funds committed to these SBIR grants support a variety of biotechnology projects, examples of which are given in the first report I submitted, the one entitled "The NIH Role in the Support and Application of Biotechnology Research."

- The Federal Technology Transfer Act of 1986 (PL 99-502), which is designed to promote the transfer of Government-developed technology into the private sector, mandates a policy which is consistent with the desire of NIH to further collaboration between its intramural research programs and the biotechnology industries. Since 1985, NIH has had a policy permitting intramural scientists to consult with industry. This is seen not just as an opportunity for an intramural scientist to share his or her most recent experiments with industry on a selective basis, but rather as an opportunity for industry to tap that scientist's general knowledge and expertise in a field of particular interest. In addition, NIH is encouraging the possibility of more scientists from industry working in its intramural laboratories for appropriate periods of time, activities which should lead to further collaborations. As a result of the Federal Technology Transfer Act of 1986 and the ensuing Executive Order 1259, the Department of Health and Human Services has delegated to NIH the authority for its laboratories to enter into licensing and cooperative research agreements with industrial organizations. The number of scientists working within the NIH's own laboratories who have obtained patents and are collaborating with industry is growing. Currently, there are 124 ongoing licenses and the total royalty collections by the National Technical Information Service of the Department of Commerce from these licenses was over $4 million in Fiscal Year 1987.
- NIH representatives are also working closely with both biotechnology firms and local governments in the Washington-Baltimore area, such as the Montgomery County High Technology Council, to assist and promote the biotechnology industry. Attracted, in part, by the proximity to

NIH, there are now approximately 130 biotechnology companies in this region--ten percent of the Nation's total--employing over 3,300 workers.

To facilitate further technology transfer, NIH is establishing an Office of Invention Development that will, as one function, serve as a broker to match scientists with industrial concerns based on shared research and development objectives.

Finally, I would emphasize that the Administration does concur with the goals of H.R. 4502 and S. 1966 and has already a mechanism established to achieve the outcomes these bills seek. We believe creating more commissions or advisory bodies only weakens our efforts and makes our ongoing process less efficient. Moreover, we have been advised by the Justice Department that certain provisions of the legislation present serious constitutional problems. Justice will be reporting their veiws to the Committee shortly.

I know that all of us here today would agree that the excitement of the ongoing biological research endeavors has never been greater, that the opportunities for commercial biotechnological applications are growing and that there will be an enormous impact of such applications on the improvement of human health, on characterizing and understanding our genes, on increased production of food, on improving the environment, and on the Nation's economy. The NIH expects to play an even larger and more critical role, both in the support of the basic research that makes these applications possible, and in encouraging and enhancing commercial applications. Equally important, we will continue to further emphasize both informal and formal collaborations and cooperation with other Federal agencies and, as appropriate, on an international level.

Thank you for giving me the opportunity to describe the activities of the NIH in regard to biotechnology. I would be happy to answer any questions.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

The NIH Role in the Support and Application of Biotechnology Research

Ruth L. Kirschstein

Ruth L. Kirschstein, M.D.
Director, NIGMS

January 1988

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health

NIH Role in the Support and Application of Biotechnology Research

James B Wyngaarden

James B. Wyngaarden, M.D.
Director, NIH

January 1983

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health

The NIH Role in the Support and Application of Biotechnology Research

William F. Raub, Ph.D.
Deputy Director, NIH

January 1988

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health

The NIH Role in the Support and Application of Biotechnology Research

Table of Contents

Executive Summary

Introduction 1
 Background 2
 NIH Contributions to the Advancement of Biotechnology . . . 3
 Reassessing the NIH Role 6
 Promoting University-Industry Cooperation. 8
 Co~~l~~laboration with Industry. 10
 Research Training and Fellowship Programs in Biotechnology . 12
 Research Resources 13
 Looking Ahead 13

Appendices

A. NIH Funding of Research Related to Biotechnology
B. Research Advances Related to Biotechnology
C. Partial List of State-Sponsored Biotechnology Programs
D. Small Business Innovation Research (SBIR) Program Grants Funded by the National Institute of General Medical Sciences, Fiscal Year 1987

The NIH Role in the Support and Application of Biotechnology Research

Executive Summary

In Senate Report No. 100-189, the Committee on Appropriations requested that the NIH prepare and submit a report on activities to encourage collaborations in biotechnological research between academia and industry and between the NIH and industry. The Committee further requested that the NIH report on efforts to assist in the transfer of NIH-sponsored basic research findings to biotechnology industries with a view to accelerating the development of commercial products. The following report is submitted in response to those requests.

The biotechnology enterprise is largely due to the substantial investment in basic research on molecular and cell biology made over the past several decades through the NIH. NIH provided nearly $2.3 billion for biotechnology-related research in Fiscal Year 1987 within academic institutions and industries, and within the NIH intramural laboratories. Much of this research involves cooperative efforts between NIH intramural laboratories and biotechnology companies; between academia and biotechnology firms; and between state-sponsored biotechnology centers/programs and relevant industries. Biotechnology companies funded by the NIH Small Business Innovation Research Program are important contributors in all three types of relationships.

The aforementioned activities notwithstanding, NIH acknowledges the increased opportunities in the biotechnological arena and has sought the advice of representatives of government agencies, universities, and biotechnology companies in assessing its role and formulating its future strategy. Informed by these consultations, NIH will: (1) provide support for intramural and extramural biotechnology-related research and promote cooperative linkages between NIH-supported research programs and biotechnology industries; (2) support research training of critically needed biotechnological personnel; (3) improve the infrastructure for biotechnology research; (4) expedite the transfer of basic scientific discoveries to specific applied research and development activities; and (5) continue to seek the advice of biotechnology scientists and administrators on broad strategies to facilitate more effectively the flow of basic research discoveries into commercially-oriented research and development on new or improved biotechnology products and services.

The NIH Role in the Support and Application of Biotechnology Research

Introduction

In its report (Senate Report No. 100-189) on the Fiscal Year 1988 Appropriations for the Department of Health and Human Services, the Committee on Appropriations stated:

> "The Committee has also noted the investment being made by other countries in areas critical for the commercial development of biotechnology products. Significant barriers to further development of this new technology have been identified by industry and the research community. These include the need for additional research in protein engineering and other types of what has been termed applied biotechnology research. It is also the sense of the Committee that cooperative research relationships between universities and industry have significantly aided the transfer of technology to private industry and have encouraged new and innovative research and commercial initiatives.
>
> The Director of the NIH is, therefore, directed to recommend to the authorizing and appropriating committees, by no later than February 1, 1988, a program to encourage cooperative university-industry applied biotechnology research. Such research should have broad applications and relevance for the diverse areas of commercial biotechnology. The Committee expects the Director to consult with interested university and industry groups in developing his recommendations." (page 84)
>
> and
>
> "NIGMS also contributes to progress in biotechnology by providing researchers with important resources. Among these is GenBank®, a computerized data bank that stores, catalogs, and distributes genetic sequence data. GenBank® enables scientists to study similarities between the sequences of different genes and to examine the role of mutation in disease states. This GenBank® resource permits researchers to keep up with the explosion of information in this field. The Committee has added $4,000,000 to enhance NIGMS efforts in the expanding area of biotechnology information handling.

> The Committee is not satisfied with the efforts of NIGMS and NIH generally to encourage and assist the private sector in commercializing the many advances and discoveries made as a result of the intramural and extramural basic research funded by NIH. We cannot afford to fund billions of dollars of research only to have the results commercialized by foreign countries and sold to the United States to further aggravate our balance of trade. The Committee directs that a report be submitted to the Senate Committee on Appropriations by January 15, 1988, detailing what additional NIH programs or activities are needed to help ensure that the findings of NIH basic research are commercialized by U.S. Firms." (page 113)

The National Institutes of Health (NIH) has been granted approval to provide a single response to the above-mentioned requests. Accordingly, the following report has been prepared by NIH, an agency of the Public Health Service, the Department of Health and Human Services, in response to the two requests of the Committee on Appropriations.

Background

In a 1984 report on commercial biotechnology, the Office of Technology Assessment (OTA) determined that three key factors--government funding of basic and applied science, adequate numbers of trained personnel, and availability of funds for industrial development--influence a country's competitive position in world markets. Support of basic research, in particular, is critical to maintaining the science base upon which a technology rests and in stimulating advances in that technology. Former Congressman Donald Fuqua addressed this fundamental issue in the Chairman's Report to the U.S. House of Representatives Committee on Science and Technology, Ninety-ninth Congress, when he observed that "the basic research being done today will, in turn, be the foundation for many of our technological advances five, ten or fifteen years from now."

Nowhere is this more evident than in the "new biotechnology." As defined by OTA, biotechnology is "any technique that uses living organisms (or parts of organisms) to make or modify products, to improve plants or animals, or to develop microorganisms for specific uses." Although man has harnessed microorganisms for thousands of years--such as in fermentation processes for making wine, beer, cheese, bread, and yogurt--the new biotechnology allows the analysis and highly specific manipulation of the genetic composition of living organisms.

This technology, therefore, offers previously unimaginable opportunities to unlock the secrets of living systems and the subsequent application of this basic scientific knowledge to research and development leading to the production of commercially significant products.

The competitive advantage that this country currently holds in biotechnology is in large part due to the substantial investments in basic research made over the years through the NIH. NIH support can be separated into two categories. The first is basic research directly related to biotechnology, which refers to techniques such as those for genetic manipulation, DNA cloning, the isolation and detection of DNA, the creation of hybridomas and the production of monoclonal antibodies, and the computer analysis of DNA and protein sequences. The second category relates to the broad research base underlying biotechnology, which includes studies in the fields of genetics, cellular and molecular biology, immunology, virology, chemistry, and pharmacology. Overall, NIH provided almost $2.3 billion for biotechnological research in Fiscal Year 1987, of which about $0.8 billion was in basic research directly related to biotechnology and about $1.5 billion was in the more broadly based biomedical science area (Appendix A).

NIH Contributions to the Advancement of Biotechnology

Research performed with NIH support is done either intramurally within the NIH laboratories or at academic institutions or research institutes, through a system of grants and contracts. For the past five years, the NIH has also supported research through the Small Business Innovation Research (SBIR) awards program. This program is designed to stimulate research by small industrial concerns. These grants are intended to: (a) stimulate technological innovation; (b) use small business to meet federal research and development needs; and (c) increase private sector commercialization of innovations derived from federal research and development.

A detailed description of specific biotechnological projects supported by the various Bureaus, Institutes and Divisions at NIH is given in Appendix B.

NIH supports and/or conducts a number of research projects involving biotechnology. These studies include the elucidation of

DNA structure; molecular cloning of complex genomes; methodologies for DNA synthesis; site-specific mutagenesis; chemical synthesis of DNA probes; the discovery and use of restriction endonucleases; methodologies for the detection, separation and characterization DNA; posttranscriptional RNA splicing; protein synthesis and posttranslational processing, modification, transport and secretion; protein structure and design; hormone and cell surface receptor molecules; hybridoma technologies and monoclonal antibody production; molecular virology; tissue and cell culture methodologies; and informatics related to gene mapping and DNA sequencing. The extraordinary coalescence of the knowledge derived from basic science and contemporary technologies of NIH-sponsored studies has already made possible many advances in biotechnology. These include the chromosomal localization of specific genetic sequences linked to the occurrence of certain human diseases (i.e., cystic fibrosis, familial Alzheimer's disease, a form of colon cancer, a form of manic-depressive illness, Huntington's disease, Down syndrome, diabetes, hemophilia A and B, sickle cell anemia, and color blindness). In fact, presymptomatic prenatal tests have been developed for the diagnosis of Huntington's disease, cystic fibrosis, and a form of muscular dystrophy in some families. The products of basic molecular genetic research have enabled biotechnology firms to produce large quantities of human growth hormone, human insulin, tissue plasminogen activator to treat heart attacks, and Factor VIII to treat one form of hemophilia. The recent success of NIH grantees in developing a new electrophoretic system for separating much larger DNA fragments than was previously possible should now permit the cloning and, ultimately, the sequencing of entire human disease-related genes. This capability will considerably advance efforts to understand many human genetic diseases.

Studies of genes involved in the development of white blood cells have increased our understanding of lymphoma, a type of blood cell cancer. Several biotechnology firms have developed tests to detect these genes that permit physicians to determine what cell type is responsible for a given case of lymphoma and thereby aid in the selection of the most appropriate therapy.

New techniques for DNA cloning and genetic manipulation have also enabled scientists to produce enough specific viral products for studies of the structure and function of certain viruses. This is a first step toward designing and/or modifying antiviral drugs. Such an approach is now being taken by six teams of NIH-supported researchers who are conducting research on structural biology applied to the problem of targeted drug design for the treatment of AIDS. Two of these research teams are, in fact, based at commercial firms that have substantial biotechnological operations.

NIH scientists and grantees have made major advances in understanding a class of biologically active proteins, called biological response modifiers, that have dramatic effects on cellular physiology, wound healing, blood vessel formation, and the immune system. A number of biotechnology companies have cloned the genes for different biological response modifiers and are now exploring the pharmacological properties of the proteins specified by these genes. For example, studies are under way on gamma interferon as a treatment for malaria, the role of transforming growth factor alpha in the promotion of wound healing, and the stimulation of the immune system by several forms of interleukin. One biological response modifier, interferon alpha, has already been approved by the Food and Drug Administration as the treatment of choice for an otherwise fatal form of leukemia called hairy cell leukemia.

It is now clear that most of the molecular, cellular, physiological, and organismal phenomena can be understood at the genetic and protein level, thus making it possible for the frontiers of biotechnological exploration spawned by NIH to also be of enormous importance in the agricultural and environmental sciences. As a result, biotechnology firms have developed a number of materials which will be useful in these arenas. Among these are: bacterial strains modified by recombinant DNA techniques to be resistant to frost; genetically engineered bacteria with increased capacity to fix nitrogen and thus improve the fertility of the soil; bacteria into which a gene for a toxin has been inserted with the expectation that the toxin will control insect damage to plant root systems; livestock modified to increase reproductive capacity, weight gain and growth rates; and animal systems, using recombinant DNA technology, to produce large quantities of protein products useful for a variety of medical and industrial purposes.

Another major NIH contribution to the advancement of biotechnology has been the agency's early involvement in guiding this new technology toward public acceptance. NIH became involved in policy formulation for the conduct of this new science in 1974, when few people besides biological scientists knew very much about the promises and potential pitfalls of recombinant DNA research. NIH was the first Federal agency to develop safety guidelines for recombinant DNA research. The initial version of the NIH Guidelines for Research Involving Recombinant DNA Molecules, issued in 1976, specified the safeguards to be utilized in the conduct of research; stipulated the administrative requirements of the sponsoring institution; and enumerated the oversight and advisory roles of the Recombinant DNA Advisory Committee and the administrative duties of the Office of Recombinant DNA Activities. Informed by experience in the conduct of recombinant DNA research and using increased understanding of potential hazards, the Guidelines were further revised in 1978 by exempting classes of experiments shown to pose no novel hazards; clearly delineating the roles and responsibilities of the sponsoring institution, principal investigator, the NIH, and the Advisory Committee; expanding the Advisory Committee membership to include nonscientists; and broadening the representation on the local Institutional Biosafety Committees. Based on evolving information related to hazards, the Guidelines were subsequently revised in 1982, 1983, 1985, and 1987 to provide for an essential but nondisruptive set of regulatory provisions. This approach now serves as a model for similar bodies in the areas of biotechnology specific to the interests of other government agencies.

Reassessing the NIH Role

In light of the rapid growth of biotechnology in the 1980's, NIH has undertaken a reassessment of its role in this area. The centerpiece of this effort was a meeting of the Advisory Committee to the NIH Director in June 1985, at which participants drawn from government agencies, universities, and biotechnology companies discussed the need to develop a national science policy for biotechnology. Among the issues raised were:

° The need to maintain federal support for research and research training to increase the base of fundamental knowledge and assure an adequate supply of trained personnel;

° The creation of incentives to encourage the investment of private capital in biotechnology research and development;

° The enactment of patent and intellectual property laws that would further encourage innovation;

° The promulgation of regulatory policies that provide adequate safeguards without stifling scientific and commercial progress; and

° The introduction of export laws that encourage equitable international exchanges while preserving ethical standards and national security interests.

Clearly, many of these issues fall outside NIH purview. In fact, other components of the federal government as well as state and local governments are better able to create the legislative, regulatory, economic, and social environments needed to promote the growth of U.S. biotechnology. The majority of the participants at the 1985 meeting felt that NIH can contribute best to the success of the U.S. biotechnology industry by sustaining its intensive support for basic research and, in particular, research training in such underlying areas as molecular biology, genetics, and immunology. It should be noted that this basic research agenda of NIH in biotechnology is shared with other federal agencies which support basic research (NSF, NASA, and NOAA), mission-specific research agencies (DOE, USDA, and DOD) and regulatory agencies (EPA and FDA).

At the June 1985 meeting, one industry representative warned that moving NIH closer to development would eventually shrink the pool of knowledge from which industry draws. He also noted, that unlike practices in some other countries, investments in developmental activities in the United States are made by the private sector, and he felt that these investments are expanding as noted in Biotechnology (U.S. Department of Commerce, International Trade Administration, 1984).

There was a consensus that one of the most crucial issues facing the biotechnology industry is the dearth of appropriately trained scientific personnel. NIH spends about $60 to $70 million a year to train research scientists in skills related to biotechnology. However, the supply of scientists who possess general knowledge in the areas of molecular biology, molecular genetics, chemistry, virology, immunology, and biophysics is being rapidly outstripped by the needs of industry and academia. A 1985 survey of 138 American biotechnology firms by the National Academy of Sciences indicated that half of the respondents were experiencing a problem with shortages of specialists. Moreover, as these firms recruit the best scientists from academia, there is a growing shortage of teachers to prepare the next generation of basic biomedical scientists.

Following the June 1985 meeting, NIH has undertaken a number of activities related to biotechnology. An NIH-wide committee on biotechnology activities has been established. This committee is working with other federal agencies such as the National Science Foundation and the Departments of Agriculture, Energy, and Defense to make each organization aware of the others' biotechnology-related activities. The committee is also compiling inventories of the biotechnology-related research training activities of NIH components and of the patents in biotechnology areas issued to NIH-supported investigators and institutions. It should be noted that NIH actively encourages universities and private companies to patent and retain the title to inventions made with NIH support with the understanding that a substantial portion of such royalties as may accrue is invested in research and education. For products developed by NIH intramural scientists, NIH offers licensing rights to firms willing to undertake the marketing of these products.

Promoting University-Industry Cooperation

As the new biotechnology has emerged, so have new partnerships between the developing industries and universities, the institutional sites for most NIH-funded extramural basic research relevant to biotechnology. These interactions, established between research universities and chemical, agricultural, and pharmaceutical firms, range from informal exchanges of information and consulting arrangements to research contracts, formal partnerships, and the creation of private corporations.

Perhaps the best known of these relationships are the multimillion-dollar arrangements between: (1) the Hoechst Company, a West Germany pharmaceutical firm, and the Massachusetts General Hospital; (2) the Monsanto Company and Washington University in St. Louis, (3) the Dupont Company and Harvard University, and (4) the Whitehead Institute and the Massachusetts Institute of Technology. However, there are many other university-industry biotechnology research programs encompassing: (a) industry-sponsored university research; (b) cooperative industry-university research; (c) joint commercial ventures; (d) research consortia; and (e) biotechnology research training centers.

According to a 1984 survey by the Center for Health Policy and Management at Harvard University, about 46 percent of biotechnology firms fund research in universities by investing in intellectual capital. The study found that these companies believe that their relationships with universities "help keep the firms current with important research, . . . reduce the cost of mounting R & D programs in new fields, . . . provide training and staff development for company scientists, and . . . enhance the firm's public image."

Equally important, as reported at the November 2, 1987 National Conference on "Collaborative Initiatives in Biotechnology: Building Federal/State Partnerships," 33 states have allocated funds for biotechnology programs/centers through various mechanisms. These centers have an average Fiscal Year 1987 budget of $2 million (50% from the State government and 50% from Federal agencies), some participation by industry and 70% are affiliated with the basic science departments of research universities. Undoubtedly, the formation of these state-sponsored biotechnology programs would not have been possible without the NIH-sponsored basic scientific base in the affiliated universities and the recent support by the NSF through its centers programs. A full report on the state-sponsored biotechnology centers is contained in Appendix C. Regarding the NSF efforts, a Biotechnology Process Engineering Center was established under the Engineering Research Centers Program at the Massachusetts Institute of Technology (MIT) in 1985. The MIT Center has research foci related to: (a) biological principles in mammalian protein production; (b) engineering principles in protein production; and (c) downstream processing in biotechnology.

Focusing on concepts in the manufacturing of complex therapeutic proteins, this center program involves the research participation of 43 biotechnology companies as well as multidisciplinary biotechnology training activities. The NIH participates in the MIT Center by providing support of predoctoral training through the National Institute of General Medical Sciences and the National Cancer Institute. The research programs of the aforementioned biotechnology centers will be further advanced by the recent award by the NSF of 20 biological center programs devoted to the development of sophisticated instrumentation for research in biotechnology and environmental biology.

NIH supports the interaction of universities with industry as long as safeguards against conflicts of interest are maintained and government-supported research results are disseminated freely. NIH awards grants to institutions in support of investigators who have meritorious proposals, regardless of whether the research will be done at a university, a private company, some combination of the two, or involves support by another federal agency. All evidence indicates that this arrangement is working well for both universities and the biotechnology industry whether it is a part of the private sector or is state-sponsored.

Collaboration with Industry

Quite understandably, there is substantial interest in the nature and scope of collaborative relationships between NIH, its academic grantees, and biotechnology companies. To reiterate, this interest is primarily due to the remarkable basic science achievements that have occasioned commercial interests in marketing the products of biotechnology; a desire to enhance the transfer of research findings to commercial applications; and the desire to utilize, effectively, federal biomedical research funds not only for basic research but also to support private industry in the translation of such research to the development of products. The special interest of NIH in promoting collaborations with the biotechnology industry has had a number of manifestations in the past 2 years. Contacts have been established with many biotechnology companies as well as with the Industrial Biotechnology Association, the Association of Biotechnology Companies, and the Society for Industrial Microbiology, organizations that represent the industry. Major briefing sessions for chief executive officers of biotechnology firms have been held so that they could become more familiar with NIH programs. A two-day seminar was held at NIH and was cosponsored by NIH and other groups so that industry scientists could visit NIH laboratories and meet leading intramural researchers.

While not strictly biotechnology, one recent example of industry cooperation is the development of azidothymidine (AZT) as a treatment for some cases of AIDS. NIH intramural scientists developed the technology for working with live AIDS virus and for determining whether a given drug might be effective against the disease. In the course of a program of screening potential anti-AIDS drugs, the scientists found that AZT, a drug submitted for testing by the Burroughs Wellcome Company, inhibited the AIDS virus. NIH performed the pharmacological studies of the drug and the clinical trials of its effectiveness, and has now established an AIDS treatment evaluation network for the testing of this and other drugs.

Another successful collaboration between NIH scientists and a private firm, Integrated Genetics, Inc., resulted in the first report of the production of a biologically active human therapeutic protein in the milk of laboratory mice. This research shows the feasibility of using animal milk as a source for the production of large quantities of certain therapeutic proteins that are difficult and expensive to make using current techniques. Integrated Genetics will now test this technology in animals that produce larger quantities of milk, such as sheep, cows, and goats.

Top NIH administrators are currently working with the Pharmaceutical Manufacturers Association and the Montgomery County (Maryland) High-Technology Council on joint initiatives in biotechnology. One such effort is NIH cosponsorship of, and participation at, a conference on "Collaborative Initiatives in Biotechnology." This meeting, held in early November 1987, brought together, for the first time, the directors of biotechnology research centers, the state and local officials charged with developing and funding these centers, industry representatives, and interested federal officials. NIH staff are also participating in a forum on drug development and regulation designed to encourage interactions in this area among government, industry, and universities. Topics of discussion have included manpower needs, ways of enhancing innovation, and the new drug approval process.

As mentioned above, through its Small Business Innovation Research (SBIR) Program, NIH supports the private sector in its research and development activities and aids in the commercialization of innovations, many of which are derived from federally supported research. As required by law, in Fiscal Year 1987, NIH set aside $61 million for the SBIR Program. As shown in Appendix D, a considerable fraction of the funds committed to SBIR grants sponsored by the National Institute of General Medical Sciences supported a variety of biotechnology projects.

The Federal Technology Transfer Act of 1986 (PL 99-502), which is designed to promote the transfer of Government-developed technology into the private sector, mandates a policy which is consistent with the desire of NIH to further collaboration between its intramural research programs and the biotechnology industries. In fact, several NIH programs have been developed which offer potential assistance to biotechnology companies. Under a 1985 NIH policy, intramural scientists may consult with industry--following certain guidelines regarding conflicts of interest--and receive compensation for their work. This is seen not just as an opportunity for an intramural scientist to share his or her most recent experiments with industry on a selective basis, but rather as an opportunity for industry to tap that scientist's general knowledge and expertise in a field of interest to the industry. Heretofore, it had not been possible for an NIH intramural scientist to have any kind of continuing contact with industry in this way. In addition, NIH is encouraging the possibility of more scientists from industry working in its intramural laboratories for appropriate periods of time, activities which should lead to further collaborations.

NIH has also recently established policies for "joint ventures" with commercial firms under explicit patent and licensing agreements. In addition, NIH is developing a royalty return schedule for intramural scientists (inventors); has established a Patent Policy Board; is considering the creation of a Division of Invention Development to handle invention reporting, patent applications, and license decisions; and is encouraging the formation of cooperative R & D agreements between NIH and biotechnology companies. All of these efforts will permit the pooling of resources and expertise under well-defined conditions and thereby facilitate the transfer of basic science findings to commercial R & D activities.

Research Training and Fellowship Programs in Biotechnology

NIH remains committed to research training--and, where appropriate, retraining--as a primary means of providing the scientific talent that will fuel the growth of biotechnology. One of the most fertile training grounds is NIH itself--specifically, its intramural program. To capitalize on this resource, last year NIH and the National Research Council, of the National Academy of Sciences, created a research associateship program in biotechnology to provide postdoctoral scientists with additional research training in biotechnology on the NIH campus. This program currently trains about 45 scientists who work in NIH laboratories for periods of 1 to 3 years.

In the extramural area, as indicated above, NIH is cooperating with NSF in the support of the biotechnology program at MIT which is training chemical engineers and biologists in areas of molecular genetics, bioprocess engineering, protein engineering, and cell culture and hybridoma technologies. Recently, the National Institute of General Medical Sciences of NIH initiated a molecular biophysics predoctoral research training program. This program, which will focus on the application of physics, mathematics, and chemistry to problems of biological structures at the molecular level, was formulated in response to the acknowledged manpower needs for protein engineering, i.e., protein structure determinations, computerized molecular modeling, and the redesign of existing and commercially important proteins using genetic engineering,. In this regard, NIH, through the programs of various Institutes, is committed to the view that continued commercialization of biotechnology depends on adequately trained scientific and technical personnel in molecular biology, genetics, virology, biochemistry, cell biology, immunology, pharmacology and biophysics, areas which constitute the scientific base that undergirds this new technology.

Research Resources

Acknowledging that a strong research infrastructure is essential to present and future advances, NIH supports certain activities that provide important resources to scientists at universities and commercial firms, particularly biotechnology companies. These include the Genetic Sequence Data Bank, known as GenBank®, which collects, maintains and distributes information on known DNA sequences; the Human Genetic Mutant Cell Repository, which collects, establishes, maintains, and distributes highly characterized cell cultures from people with biochemical genetic disorders and chromosome aberrations; the Protein Identification Resource, which maintains a very comprehensive protein sequence database designed to provide access to known proteins and to identify new structures; BIONET, which provides data analysis in molecular biology and biotechnology; the American Type Culture Collection, which serves as a national repository and distribution center for a collection of microorganisms and cell cultures, including tumor cell lines; the Hybridoma Data Bank, which acquires, stores, and distributes both hybridoma cell lines and information about hybridomas and monoclonal antibodies which have been produced around the world; and the Human DNA Probe Repository, which acquires, stores, and distributes cloned human genes, DNA probes, and human chromosome materials to molecular biologists and biotechnology organizations throughout the United States.

Looking Ahead

As it has done extensively over the past several decades, NIH will continue to support basic biomedical research and research training in those disciplinary and multidisciplinary areas essential to advancement of the biomedical knowledge base.

In this way, NIH will continue its unique role in elucidating the basic mechanisms, formulating the concepts and establishing the methodologies so crucial to future biotechnological breakthroughs and commercial achievements. Among these activities, NIH will specifically:

(a) continue to support intramural research programs, such as those described in Appendix B, and seek collaborative links with biotechnological industries, as appropriate;

(b) provide support of extramural basic and biotechnology-related research at universities and industries, thereby advancing the knowledge base and assisting university, university-industry, and state-sponsored biotechnology programs;

(c) continue its role as the premier federal agency making provision for the research training of critically needed biotechnological personnel, including the recently initiated interdisciplinary research training program in molecular biophysics;

(d) initiate a research focus in molecular pharmacology designed to elucidate the molecular mechanisms of anesthetic action;

(e) continue programs of the Division of Research Resources to support major high technology: resource instrumentation, research facilities, models and materials, data handling and manipulation, and resources used in biotechnology-related research.

(f) advance a component of infrastructure by initiation of a program on computer-based representation and analysis of molecular biology data;

(g) initiate a research program to characterize complex genomes with the objective of establishing the relationships within genomes (including the human genome) and using the resulting information for the diagnosis and treatment of human diseases;

(h) promote cooperative research ventures between NIH intramural scientists and biotechnology industries;

(i) continue to support biotechnology firms through the Small Business Innovation Research Program;

(j) establish, by the National Heart, Lung and Blood Institute, Programs of Excellence in Molecular Biology. Each Program of Excellence will combine contemporary molecular biological techniques with the more conventional research methodologies in order to provide a multidisciplinary approach to study and elucidate fundamental biological principles of cardiovascular and pulmonary system development, organization, structure, function, and pathological disease processes. In addition, a Program of Excellence in Molecular Biology will provide opportunities for investigators new to the field of biotechnology to become skilled in the experimental strategies, approaches, and techniques of molecular biology and their application to cardiovascular, pulmonary, and related hematologic research problems.

(k) continue efforts to expedite invention reporting, patenting, and license processes so as to facilitate the transfer of basic science discoveries to relevant biotechnology R & D activities; and

(l) continue to consult with the biotechnology industry and the various biotechnology association officials on collaborative mechanisms to decrease the otherwise sharp boundaries between the roles and activities of NIH and of the industries, and thereby more effectively enhance the opportunities presented by the nation's biotechnology enterprise.

NIH will, in the future, undoubtedly play a larger role in biotechnology, particularly in facilitating intergovernmental collaborations. This effort will be enhanced by the leadership of the NIH Director, Dr. James B. Wyngaarden, recently appointed as the Chairman of the Biotechnology Sciences Coordinating Committee of the Office of Science and Technology Policy. Among the plans under consideration is the sponsorship by NIH of a series of meetings of state-sponsored biotechnology organizations with a number of Federal agencies such as NIH, the United States Department of Agriculture, the Department of Energy, the National Science Foundation, and the Department of Defense, and of a convocation, possibly under the auspices of the National Academy of Sciences, of prominent scientist-statesmen, industrial scientists, university researchers, and government administrators. Such a group would be expected to develop a strategy to best take advantage of the burgeoning opportunities in biotechnology and retain the preeminence of the United States in this field. The aforementioned efforts to develop strategies will be augmented by consideration of the findings and recommendations of the forthcoming Office of Technology Assessment's report on "New Developments in Biotechnology." This report, for which NIH staff members have served as reviewers and observers at the various panel/committee meetings, will be of enormous utility. It will address biotechnology issues such as ownership and patents of human tissues and cells; public perceptions of biotechnology; genetically engineered organisms in the environment; federal government, private sector, and state/local agency investments in biotechnology; and regulatory issues. Moreover, as areas of biotechnology continue to flourish, NIH will actively seek the formal and informal advice of biotechnology industry scientists and administrators on a range of issues including: (1) sustaining support for the basic biomedical research on which the biotechnology is based, (2) establishing closer and more effective industry-NIH research linkages, (3) the removal of disincentives to rapid transfer of basic scientific findings to R & D activities, and (4) the removal of potential regulatory hindrances to biotechnological innovations.

NIH is committed to adding to the fundamental biomedical knowledge base and to ensuring that this knowledge is translated into applications which will improve the health of the nation as well as enhance its economic growth.

APPENDIX A

NATIONAL INSTITUTES OF HEALTH
BIOTECHNOLOGY FUNDING

(Dollars in Thousands)

	FY 1987 Actual			FY 1988 Appropriation		
	Directly Related	Broader Science Base	Total	Directly Related	Broader Science Base	Total
NCI	$288,443	$357,145	$645,588	$301,419	$372,286	$673,705
NHLBI	43,295	126,685	169,980	44,900	131,400	176,300
NIDR	12,475	9,528	22,003	12,687	9,672	22,359
NIDDKD	55,130	191,530	246,660	57,760	200,635	258,395
NINCDS *	20,419	157,437	177,856	21,815	172,258	194,073
NIAID	176,994	120,009	297,003	186,406	124,695	311,101
NIGMS	153,123	202,977	356,100	169,268	224,380	393,648
NICHD	47,873	113,342	161,215	51,800	122,700	174,500
NEI	21,870	15,825	37,695	22,958	16,768	39,726
NIEHS	1,456	13,100	14,556	1,505	13,541	15,046
NIA	10,180	10,148	20,328	11,119	11,082	22,201
NIAMS	16,861	32,042	48,903	17,805	33,755	51,560
DRR	34,349	61,832	96,181	36,854	65,605	102,459
Total, NIH	$882,468	$1,411,600	$2,294,068	$936,296	$1,498,777	$2,435,073

* Estimated FY 1987 Actual

APPENDIX B

Research Advances Related to Biotechnology

The descriptions which follow represent selected projects among the research activities supported by NIH in biotechnology-related areas. These descriptions, drawn from the various Bureaus, Institutes and Divisions of the NIH, are organized by broad research areas.

Molecular Genetics, DNA Cloning, Genetic-Based Diagnosis

- Much of biotechnology involves producing human and other proteins in foreign organisms such as yeast or bacteria. However, problems can arise in the use of such host systems due to biological differences between the organism from which the gene of interest is derived and the host used to produce large amounts of the gene's protein product. These problems are related to gene expression, nucleic acid and protein stability, and maintenance of the activity of the gene in host cells.

  Many grantees of the National Institute of General Medical Sciences (NIGMS) are providing new information that has important implications for biotechnology through their studies of basic biological processes. Two examples come from NIGMS-supported research on gene expression, in particular on the process by which information contained in RNA is translated into protein. One of these projects is focusing on the initiation of translation; the other is investigating the addition of amino acids to a growing protein chain. The scientists involved have found that the efficiency of each stage of protein synthesis appears to be influenced by the detailed structure of the genetic material surrounding the sequence being translated. Although the rules governing these so-called "context effects" are quite different in the two cases, understanding these and other aspects of translation--and learning how they vary from one organism to another--will improve scientists' ability to control gene expression in host systems. This, in turn, will lead to improvements in the manufacture of products made by biotechnology.

- One of the most exciting developments in basic genetic research conducted over the past two decades is a technique that enables scientists to follow the inheritance pattern of specific differences in DNA sequences in families in which a genetic disease has been found and for which neither the gene nor the biochemical defect is known. If linkage between the occurrence of an inherited illness and a specific DNA sequence (called a marker) is observed, then the general location of the gene causing the particular illness can be identified. Eventually, this will enable researchers to isolate the specific gene and determine its protein product. This technique has already been used to identify markers associated with the genes for a number of diseases, including Huntington's disease, cystic fibrosis, Duchenne muscular dystrophy, and renal cell cancers. This year, an NIGMS grantee was involved in the identification of a marker for susceptibility to a form of manic-depressive illness. This finding represents the first clear evidence of a possible genetic basis for a major psychiatric disorder.

- Using recombinant DNA technology to make DNA probes, at least one gene related to familial Alzheimer's disease has been linked to human chromosome 21. Current research supported by the National Institute on Aging (NIA) and the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) is focused on isolating the gene, identifying the nature of its product, and determining how the gene and its product are involved in the loss of brain cells and memory in patients with Alzheimer's disease. Once that has been accomplished, it may be possible to develop an intervention to prevent these losses.

- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) supported researchers as well as NIH intramural scientists have successfully taken the first steps toward future gene therapy (the replacement of defective genes with normal ones). Several research teams have succeeded in inserting normal human genes into mouse cells in test-tube systems and then reintroducing the altered cells into the animals from which they were taken. Using recombinant DNA technology, scientists are constructing vectors that serve as delivery agents. The desired gene is spliced into the vector, which then delivers the missing or defective gene. Thus, a serious genetic defect may be corrected.

- Since many genetic disorders are fatal or extremely debilitating and have no effective treatment, studies involving gene therapy open a new avenue for the potential treatment of these disorders. A specific group of investigators supported by the National Institute of Child Health and Human Development (NICHD) is studying ways to develop safe and effective gene therapy for several genetic disorders. These include phenylketonuria, urea cycle disorders, and severe combined immunodeficiency disease. Cultured cells and experimental animal models of these diseases are being used to test methods involving recombinant DNA technology and the transfer of genes followed by attempts to detect the subsequent functions of the genes.

- NIDDK grantees are actively taking part in the intense international search for the cystic fibrosis gene. New markers have been identified that are extremely close to and tightly linked to the gene, now targeted to a small area on chromosome 7. Once scientists find the gene, researchers will begin to explore the role of the gene in causing the disease, the development of tests to identify carriers of the gene, and opportunities for more effective therapies.

- The defective hemoglobin molecule in the red blood cells of sickle cell patients leads to chronic anemia, poor resistance to infection, severe pain, and premature death. About 50,000 Americans are affected by the disease, and millions of others have closely-related blood disorders. Approaching these problems at the level of the gene, NIDDK intramural researchers are determining the control of globin genes, which produce the protein hemoglobin. One globin gene produces fetal hemoglobin, which normally is produced by the newborn infant and during the first six months of life. Since patients with sickle cell anemia produce normal fetal hemoglobin, keeping their fetal hemoglobin gene continuously "turned on" could provide sickle cell patients with their own supply of nondefective hemoglobin throughout their lives.

- The genetic locus for adult polycystic kidney disease, the most common heritable renal disease, has now been closely linked to one of the globin genes on chromosome 16. This recent finding by NIDDK researchers provides a basis for extending these studies to determine if all afflicted patients suffer from the same genetic defect and to construct a linkage map of the chromosome. The mapping of the gene and identification of bracketing markers would offer a way to diagnose the disease prenatally and presymtomatically in affected families. This research exploits recent advances in molecular genetics and should ultimately permit scientists to find the gene for polycystic kidney disease.

- NIDDK intramural researchers have cloned the gene for the mouse sperm receptor and have isolated an antibody that blocks penetration of the sperm into the egg. The antibody prevents sperm from penetrating the inner layer of the egg cell's protective coat and thus has important implications of contraception. The new clone also permits investigation into the ways egg genes create proteins like the sperm receptor. Studying egg coat proteins has led to the isolation of five monoclonal antibodies that recognize distinct areas on the egg coat and reveal the location of proteins like the sperm receptor. Very promising is the reversibility of the antibody: when antibody levels fall, fertility resumes. Further studies should resolve the efficacy of such antibodies in contraception.

° The National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) is currently funding two "centers without walls" for the study of Huntington's disease, a neurogenetic disorder. These centers conduct basic and clinical research activities directed at gaining a better understanding of the disease. At one of the centers, scientists are continuing work on the development of DNA probes, using recombinant DNA technology, for genetic material located close to the Huntington's disease gene on chromosome 4 and are creating strategies to isolate and clone the gene itself.

° NICHD has awarded a contract for the creation of a repository of human DNA probes and, as a component of the NICHD contract, the Division of Research Resources (DRR) supports chromosome-specific libraries (fragments of a complete genome separated by chromosomes). The purpose of the repository is to provide a collection of DNA probes and libraries relevant to human genetic diseases, and to distribute the probes and libraries to investigators studying these diseases. Ultimately, the repository can be expected to contain approximately 1,000 probes.

° The gene responsible for the development of retinoblastoma has been localized to a specific region of chromosome 13 by investigators working with National Eye Institute (NEI) support. Subsequent to its localization, researchers have cloned and sequenced the gene and have also determined the amino acid composition of the protein coded by this gene. Additional research has indicated that this protein may bind to DNA, suggesting that it may have a regulatory function. This research has not only provided invaluable information about the development of retinoblastoma, but also about related forms of cancer. These studies may lead to improved genetic counseling, screening, and detection, and ultimately to the development of treatment at the gene level.

- Progress continues to be made by NEI intramural researchers in the characterization of the structure of the genes that control the production of the important proteins of the lens called crystallins. The sequences for certain human and chicken crystallin genes have been nearly completed. These studies will lead to a better understanding of the normal structure, function, and regulation of the crystallin genes, as well as of the defects in gene function that may occur during the development of cataracts. Through comparisons of the composition and structure of these crystallins with the composition and structure of other proteins, these investigators have also determined that many of the crystallins were derived from enzymes, and in some cases, appear to continue to be active enzymes. These surprising findings provide important information about the evolution of the lens, but also pose interesting questions about the regulation of the genes controlling crystallin production.

- When cells are grown in culture, they will divide only a limited number of times. The cells then become quiescent and eventually senescent. Young cells can be converted to senescent-like cells by injecting them with a protein found only in senescent cells. Current NIA-supported research is focused on isolating and characterizing the protein, cloning the gene that codes for it, and then studying the control of expression of the gene to determine why and how the cells enter the senescent state.

- Because epidermal cells can now be cultured routinely, it has become possible to characterize with precision all of the major epidermal structural proteins. One of these is filaggrin, a molecule that acts to associate individual keratin filaments into larger bundles. Using cloned DNA for the filaggrin gene, researchers have managed to modulate filaggrin synthesis in a test-tube system. This achievement is an important step toward gaining greater insight into keratin diseases and developing treatment interventions.

- Collagenase is an enzyme that initiates the breakdown of collagen, the body's most abundant structural protein. The impact that excess collagenase can make is most apparent in rheumatoid arthritis, where there is destruction of cartilage, tendon, and bone, with loss of joint function. The fact that collagen breakdown can be initiated only by collagenase makes this enzyme rate-limiting. National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIAMS) supported researchers recently isolated and characterized clones for synovial cell collagenase genes. These clones were demonstrated to be identical to the genes as they exist in the genetic material of the animal models studied. The clones will be used to complete the sequencing of the collagenase gene. This will enhance our understanding of the mechanisms regulating collagenase production.

° Application of the techniques of modern molecular biology by National Heart, Lung and Blood Institute (NHLBI) intramural and extramural scientists has led to a nearly complete understanding of, and ability to diagnose, the thalassemia syndromes. The thalassemias, the most common form of which is Cooley's anemia, are inherited diseases characterized by deficient synthesis of one of the two protein components of hemoglobin, the oxygen-carrying protein of red blood cells. These two components are the alpha and beta subunits and the genes which code for these proteins have been cloned and sequenced. More than 50 different mutations in the thalassemia globin genes have been identified. Prenatal diagnosis of severe forms of thalassemia, using a biotechnological tool, DNA analysis, is now possible and has been widely applied in many areas of the world, leading to a marked reduction in the incidence of the disease.

° NHLBI intramural and extramural scientists are also studying the process of globin gene switching as it relates to the manifestations of Cooley's anemia. Fetal hemoglobin prevents anemia during gestation, but, at birth there is a normal physiological switch from fetal to adult hemoglobin and the defect in hemoglobin synthesis becomes evident in individuals with Cooley's anemia. Recent studies have focused on preventing or modulating this normal gene switch in order to prevent the disease. It has been found that several naturally occurring mutations may increase the production of fetal hemoglobin during adult life. Using recombinant DNA techniques it may be possible to take advantage of these mutations to develop therapies for Cooley's anemia.

In related research, infants of diabetic mothers have been shown to exhibit a delayed switch from fetal to adult hemoglobin production. It appears that the normal globin gene is influenced by intrauterine environmental factors that disrupt the normal developmental gene switch. A metabolic breakdown product responsible for this effect has been identified, and its concentration has been shown to be elevated in the intrauterine environment of the fetus of a diabetic mother. Such observations may lead to the discovery of substances that have valuable potential for treating Cooley's anemia patients.

- Recently, scientists working with NHLBI extramural funds developed a one-day method for the rapid detection of the genetic mutation that causes sickle cell disease. The method, based on recombinant DNA technology, is at least ten thousand times more sensitive than conventional techniques. The approach is applicable to the diagnosis of other genetic disorders in which the mutation has been localized and fully characterized.

- No treatment or preventive measure exists for Duchenne muscular dystrophy (DMD), the most frequently occurring of the childhood-onset muscular dystrophies. This situation may change, however, as a result of NINCDS-supported research in which a recently developed probe that recognizes a DNA sequence found in several boys with DMD is being tested for its ability to identify the presence of the DMD gene in others. Such studies may lead to successful strategies to prevent or treat this devastating disease.

- Studies are continuing under a grant from DRR to develop a new, improved diagnostic test system for Herpesvirus simiae B virus using recombinant DNA technology. The goal is to control B-virus infections by identifying infected nonhuman primates and potentially infected humans. The high incidence of B-virus in many colonies of nonhuman primates and the very significant human health hazards associated with this disease mandate that enhanced diagnostic techniques and other control measures be developed as soon as possible. Arrangements are currently being made to initiate collaborative studies with an industrial laboratory to facilitate progress in the development of B-virus diagnostic measures.

- In a DRR-supported study, human-derived interferon, a protein produced by biotechnological processes, has been evaluated for possible effect on pregnancy. Interferon may have widespread applications in the treatment of viral diseases and cancer. The study, in which interferon was administered to pregnant monkeys, showed that the protein can cause abortion at moderate to high dose levels. This work is representative of a trend toward greater use of monkeys to test biotechnology products because many of these products are not active in species other than primates.

Hybridoma Research, Monoclonal Antibodies, Immunology, and Virology

- Antigenic variation, or "drift," of the influenza virus is an important factor leading to the yearly outbreaks of human disease. Currently, studies of antigenic variation in influenza viruses are performed using reagents produced in mice. The National Institute of Allergy and Infectious Diseases (NIAID) is supporting research to produce human monoclonal antibodies with specificity for influenza virus antigens and to define their immunological and biological properties. These human monoclonal antibodies will be compared to mouse antibodies to determine if they both identify similar antigenic structures on the viral hemagglutinin, the molecule that is responsible for the antigenic variations in influenza. Such information is essential to the design of new strategies for the prevention of influenza by the use of potent and effective vaccines.

- An NIAID grantee is developing human monoclonal antibodies against group B streptococci (GBS), bacteria that cause life-threatening infections in the newborn. These antibodies could be a significant addition to neonatal therapy, and offer the opportunity to elucidate fundamental understanding of how an antibody protects against blood infection by GBS. In addition, the approach of constructing therapeutically useful human monoclonal antibodies against important disease-causing bacteria may be generally useful in those situations in which preformed antibodies are not present and life-threatening infection progresses more rapidly than does the immune response.

- Scientists at NIAID are using a variety of approaches in developing AIDS vaccine preparations, including the use of purified natural products of the HIV virus, products made using recombinant DNA technology, as well as products made using live vaccinia virus into which the genetic material of HIV is inserted. The first U. S. study of an experimental AIDS vaccine in human volunteers is currently being conducted by NIAID intramural scientists. The vaccine consists of the HIV envelope glycoprotein that has been produced in an insect cell system by recombinant DNA techniques utilizing a baculovirus (insect virus) expression vector. NIH scientists played major roles in developing the vaccine, which is being manufactured by MicroGeneSys, a biotechnology firm in New Haven, Connecticut. The vaccine is being evaluated for safety and immunogenicity in 81 healthy, HIV-antibody-negative homosexual and heterosexual males whose recent and current sexual behavior can be described as "low risk" for HIV infection. Once safety, immunogenicity, and optimal dosage have been established, the vaccine may undergo additional, larger-scale tests.

° A team of NIGMS-supported researchers has succeeded in developing antibodies with catalytic properties like those exhibited by enzymes. These antibodies, called abzymes, may eventually be used to destroy viruses or blood clots. If abzymes can also be designed to cut proteins at specific places, scientists may have a tool as useful for cutting proteins as restriction enzymes are for cutting DNA. This technique would be an important advance for the biotechnology industry.

° A study funded by NICHD is being conducted to evaluate the possiblity of using monoclonal antibodies to human sperm as a contraceptive agent. A number of different monoclonal antibodies have been generated against human sperm. These antibodies are currently being screened, characterized, and purified. The ability of sperm to fertilize an egg after treatment with antibodies will be assessed to determine whether antisperm monoclonal antibodies have potential contraceptive use.

° National Institute of Environmental Health Sciences (NIEHS) scientists have used highly specific monoclonal antibodies to identify and characterize cellular constituents that may serve as markers for identifying the effects of toxic compounds on the development of sperm. This work, coupled with other test-tube methods useful for assessing the mechanisms of action of reproductive toxicants, may provide information useful in the clinical management of infertility and the development of effective male contraceptives.

° Researchers supported by NEI have developed monoclonal antibodies directed against antigens present in two forms of eye cancer, uveal melanoma and retinoblastoma. These antibodies are being used to develop laboratory tests to increase diagnostic and prognostic accuracy. The researchers are also attempting to link these monoclonal antibodies to various toxins in an effort to develop a more effective means of delivering anti-cancer agents directly to tumor cells.

° An innovative method of altering enzymes is providing a novel therapy for children whose immune systems have been devastated because they do not produce an essential enzyme. Previous attempts at enzyme replacement therapy failed because the enzyme was destroyed very rapidly in the blood. Treatment with the altered enzyme now appears to be restoring immunity to these children, some of whom had been confined to living in germ-free "bubbles." Through a Small Business Innovation Research (SBIR) grant from NIDDK to Enzon, Inc., of New Jersey, the company devised a method for modifying the enzyme to keep it intact in the circulation. This exciting breakthrough is expected to be applicable to the preparation of other altered enzymes that are missing or defective in many metabolic diseases.

° Organ rejection continues to be a major obstacle to transplant success, even though immunosuppressive therapy has dramatically improved the outcome of organ transplants. The use of monoclonal antibodies to specific immune cells now offers another approach for the management of episodes of acute organ rejection. NIDDK-supported scientists are showing that these biological agents, used in conjunction with immunosuppressive drugs, can enhance the reversal of organ transplant rejection.

° NEI-supported researchers have developed immunoliposomes containing antiviral drugs for the treatment of herpes simplex virus infection of the cornea (HSV keratitis). These immunoliposomes are minute lipid (fat) sacs containing antiviral drugs linked to monoclonal antibodies directed against viral antigens. This provides the capability of delivering drugs directly to the site of infection. This research may provide an improved approach to the treatment and management of herpetic ocular disease.

° Pancreas transplantation--whole and segmental--has become increasingly successful over the last 10 years, and the use of this form of therapy for diabetes is expanding. NIDDK grantees have achieved success in certain animal studies in which monoclonal antibodies have been used to inactivate the cells responsible for triggering rejection of the transplant. This still experimental form of therapy, now just entering the initial period of human trials, may someday become a viable and routine treatment for people with insulin-dependent diabetes.

° Using monoclonal antibodies to the receptor for thyroid-stimulating hormone, NIDDK intramural scientists have resolved many clinical questions about Graves' disease, while broadening understanding of autoimmune processes. Graves' disease patients produce autoantibodies that bind to receptors for the hormone, inducing oversecretion of thyroid hormone. Intramural scientists have now characterized these abnormal antibodies, a major advance in understanding the disease. The detection of autoantibodies to these endocrine cells has given rise to new approaches to unraveling the diverse immunologic disturbances that can appear in many endocrine organs.

° Both forms of inflammatory bowel disease--Crohn's disease and ulcerative colitis--are incurable diseases of the digestive tract. Of probable autoimmune origin, these debilitating diseases afflict two million Americans. Recently, NIDDK-supported researchers developed monoclonal antibodies to unusual proteins newly isolated in Crohn's disease patients. The antibodies may prove to be valuable probes in diagnosing the disease and in ultimately pinpointing its cause.

Therapeutic Agents

° With NHLBI support, human granulocyte macrophage-colony stimulating factor, a protein which stimulates the production of white blood cells, has been produced by recombinant DNA technology and administered to AIDS patients who have very low levels of certain classes of such cells. Increases in circulating white blood cells or leukocytes were observed to be dependent on the dose of the colony stimulating factor administered. In addition, over one-half of the patients had a 50 percent or greater increase in total white blood cell count. Further studies will provide data on the relationship between the increase in number of leukocytes and the reduction in illness and death due to opportunistic infections and cancers in AIDS patients.

° In NHLBI-supported studies, two types of proteins produced by recombinant DNA technology, lung surfactant proteins and alpha-1-antitrypsin (a1AT), are being tested as replacement therapy for neonatal respiratory distress syndrome (RDS) and familial emphysema, respectively. Three types of human recombinant surfactant proteins have been synthesized, and the results of experiments performed to establish their effectiveness look encouraging. Previous clinical studies using preparations of surfactant proteins from animals have demonstrated that such therapy can produce immediate, significant, and sustained improvement in infants with neonatal RDS.

It is known that replacement therapy with a1AT purified from human plasma is an effective intervention in patients with familial emphysema. Now, NHLBI intramural and extramural investigators are evaluating the use of recombinant a1AT. Unlike the plasma-derived product, recombinant a1AT does not have certain sugars attached, which gives it a relatively short half-life and limits its benefit for patients. Direct administration of aerosolized a1AT into the lungs may circumvent this problem. This method is currently being tested for effectiveness in delivering protective levels of the drug to the lungs of affected patients.

° NHLBI-funded scientists are testing Factor VIII, blood coagulation protein, produced by recombinant DNA technology as replacement therapy for patients with the inherited disease, hemophilia. Deficiencies of Factor VIII and Factor IX cause hemophilia A and B, respectively. The genes for these factors have been cloned and sequenced, and clinical trials using recombinant Factor VIII have recently begun. The use of Factor VIII, produced by recombinant DNA techniques, rather than that derived from plasma for replacement therapy, will eliminate the occurrence of transfusion-transmitted complications, such as hepatitis and AIDS infection. In addition, the new biotechnology or molecular biology has provided valuable information on the relationship between the specific defects in the genes coding for Factors VIII and IX and the clinical severity of the resulting disease. This information has greatly enhanced both our understanding of the molecular basis of hemophilia and of the potential products that may be developed to advance the therapy of hemophilia patients.

° A major breakthrough was achieved by NIDDK intramural researchers last year by the successful treatment of chronic non-A, non-B hepatitis with alpha-interferon. It has also benefited patients with the other two forms of chronic viral hepatitis, type B and delta hepatitis. This research had led to upcoming clinical trials of this biological response modifier.

° In a landmark achievement in hematologic research, NIDDK-sponsored scientists collaborated with Amgen, a California biotechnology company, to clone the gene for erythropoietin, the major hormonal regulator of red blood cell production. This now allows the large-scale production of human erythropoietin using recombinant DNA technology. Clinical trials of the drug have shown that it can decrease anemia in patients with end-stage renal disease, leading to a tremendous improvement in their quality of life. This work also points to the possiblity of using erythropoietin to treat patients with anemia related to other disorders.

- Highly purified amounts of osteogenin, a protein bone growth factor, have been recovered from extracts of animal tissue, permitting the sequencing and ultimate synthesis of the material using recombinant DNA technology. National Institute of Dental Research (NIDR) intramural scientists are collaborating with researchers at Genentech, a California biotechnology firm, to sequence the protein. Purified osteogenin may have many important medical applications. For example, the protein applied to a base of collagen has been shown to regenerate the bony tissues of the head and face.

- Following the NIDR-supported identification of the components of mussel-adhesive protein, a naturally produced adhesive enabling salt-water mussels to adhere to underwater surfaces, American biotechnology firms have isolated and sequenced clones of the genes encoding various portions of the protein. Current research is exploring the possibility of expressing these clones in a strain of yeast with an eye to the development of methods that will allow production on a large scale. Such a synthetic material that adheres to wet surfaces would have abundant applications in dentistry, general surgery (especially orthopedics), as well as other commercial uses, such as in the shipbuilding industry.

- A new, safe pertussis vaccine, based on a modified bacterial toxin, was developed in response to growing concern about the safety of the presently-used vaccine. In collaboration with NICHD, NIDDK scientists devised the methods needed for the large-scale production of the new pertussis vaccine. With the largest biotechnology unit at NIH, NIDDK mobilized both its resources and expertise to scale up the production of the vaccine to quantities large enough for ongoing clinical trials and for possible large-scale immunization in the future.

- The Food and Drug Administration recently approved the use of tissue plasminogen activator, produced by a U.S. biotechnology company using recombinant DNA technology. Use of this drug minimizes heart muscle damage immediately following a heart attack. Blood clots that form in coronary arteries cause heart attacks by depriving the heart tissue of an adequate blood supply. "Recombinant" tissue plasminogen activator (rtPA) dissolves such clots in approximately three-fourths of patients when given intravenously within 6 hours after the onset of symptoms. Improved heart function occurs when rtPA is administered within 2 to 4 hours. Early treatment with rtPA may help reduce illness and death among the more than 800,000 Americans who suffer first heart attacks each year.

Cancer Research

- Drug resistance is a frequent cause of the failure of cancer chemotherapy. Advances in molecular biology recently have enabled scientists to begin to understand how a cancer cell that is resistant to certain drugs develops a cross-resistance to other unrelated drugs having different mechanisms of action. A glycoprotein (sugar-containing protein) associated with the outer membrane of resistant cancer cells has been identified. This membrane protein appears to act as a "pump" that continually moves toxic drugs out of tumor cells. Using the new biotechnology of recombinant DNA, scientists have isolated the gene responsible for the production of this protein, and thus the development of resistance of human tumor cells to drugs. The opportunity now exists to develop molecular probes that will detect the presence of this gene and, more importantly, allow the development of chemotherapeutic agents that are not affected by this protein pump. It also may be possible to develop drugs that specifically interfere with the function of the pump, and thus prevent or circumvent the development of multidrug resistance. Other drugs (such as verapamil, which is used to treat heart disease) that have no antitumor effects of their own can displace anticancer drugs from the membrane pump so that such a drug remains inside the tumor cell and can destroy it. Several American pharmaceutical companies are collaborating with National Cancer Institute (NCI) investigators in these studies.

- With the development of the biotechnology involving hybridomas came the ability to produce monoclonal antibodies that can react preferentially with a particular type of cancer cell. When a monoclonal antibody is attached to a toxin (poison) molecule, the resulting conjugate is termed an immunotoxin. One such immunotoxin has been used effectively in preliminary studies to treat patients with adult T-cell leukemia. Another immunotoxin has been developed that reacts specifically against cells from ovarian cancer. Preliminary clinical studies are underway to test its effectiveness in treating patients with ovarian cancer that has spread to other parts of the body.

Recombinant DNA technology has also been used to construct molecules of toxin modified in order to decrease the nonspecific side effects often associated with immunotoxins. These new molecules are then joined to specific antibodies or growth factors to produce improved immunotoxins that promise to be even more effective in cancer treatment. Several American biotechnology companies are collaborating with NCI investigators in these efforts.

° Pharmacological agents that inhibit invasion may prevent the transition of a cancer confined to a single part of the body to an invasive disease, and could conceivably be used as cancer chemotherapeutic agents. Inhibitors of tumor invasion could potentially arrest the growth of established metastases (cancers that have spread to other parts of the body), because a metastasis may need to invade locally as it grows.

Autocrine motility factor (AMF), a protein produced by certain cancer cells, has been found to play an important role in the process by which cancer cells invade distant sites in the body. AMF appears to act by stimulating the migration of tumor cells, and has been purified and partially characterized. Very small amounts of AMF can stimulate the motility of breast cancer cells, but fail to induce motility in normal white blood cells. A therapeutic agent aimed at inhibiting this factor thus should be effective against a metastatic tumor but have low toxicity for normal cells. Antibodies directed against such a motility factor or the molecules to which it binds could be used to localize metastases and even to predict the aggressiveness of a particular cancer in an individual patient. Several pharmaceutical companies are collaborating with NCI investigators in studies, using biotechnology, which are aimed at developing new anti-cancer treatments.

° Many NCI-supported clinical trials now involve the use of biological response modifiers, agents that alter the relationship of the host to the tumor. The types of cancer being treated in this way include melanoma, colorectal cancer, ovarian cancer, renal (kidney) cell cancer, Hodgkins and non-Hodgkins lymphomas, and hairy cell leukemia. Nearly all of the primary biological agents under investigation (which include interleukin-2, lymphokine activated killer cells, human monoclonal antibodies directed at colon cancer, alpha-interferon, gamma-interferon, and granulocyte macrophage-colony stimulating factor) are available as the result of the use of recombinant DNA technology.

- Recent studies have shown that uromodulin, an immunosuppressive protein originally isolated from the urine of pregnant women is produced in the kidney and probably plays an important role in regulating the circulating levels of several biological response modifiers, including interleukin-1, interleukin-2, and tumor necrosis factor. Preliminary data suggest that uromodulin is nontoxic and can protect animals from the lethal effects of a number of bacterial toxins. It soon should be possible to produce large amounts of recombinant uromodulin using recombinant DNA technology and thus be able to evaluate its clinical usefulness. This work opens up an entire area of research into the development of new, clinically useful immunoregulatory compounds, and an American pharmaceutical company is collaborating with NCI investigators in this work.

- The development of Wilms' tumor, a form of kidney cancer in children, has been associated with a deletion in a specific region of chromosome 11. DRR-supported researchers investigated the structure and function of the deletion in the development of cancer by introducing a normal human chromosome 11 into a Wilms' tumor cell line. The results indicate the existence of genetic information on chromosome 11 that can control the malignant expression of Wilms' tumor cells. Similar approaches can also be used to determine whether genes that control the malignant potential of other cancers through a similar mechanism are present on other chromosomes, such as chromosome 13 for retinoblastoma or chromosome 1 for neuroblastoma.

Biotechnology Infrastructure and Research Methodologies

- One of the rate-limiting steps in the dideoxynucleotide method for DNA sequencing is the low processivity or rapid dissociation of the DNA polymerase from the DNA. In an elegant series of studies, NIAID-supported investigators have chemically modified the bacteriophage, T7 DNA polymerase resulting in a form of this enzyme with catalytic properties ideal for DNA chain synthesis (i.e., high processivity, a rapid rate of DNA synthesis, and efficient incorporation of DNA nucleotide analogues). This T7 DNA polymerase, termed Sequenase, is now commercially produced by the United States Biochemical Corporation as the new enzyme for DNA sequencing.

- The staggering volume of molecular data and its cryptic and subtle patterns have led to an absolute requirement for computerized databases and analytical tools. The rapid expansion of data in the field has been accompanied by a proliferation of highly specialized databases, built independently from one another using dissimilar computer systems, incompatible searching methods, and having few conceptual likages between them. The National Library of Medicine (NLM) has a number of programs that are attempting to overcome this electronic "Tower of Babel."

° Computer scientists in the NLM's Lister Hill Center have built an advanced laboratory computer workstation that allows a researcher to retrieve information simultaneously from multiple biotechnology databases. The researcher may enter a question in his or her own words and have it answered with information from NIH's GenBank®, the Protein Information Resource, the Library's own MEDLINE database, as well as other information sources. The prototype will soon be made available to NIH molecular biologists for testing before it is released for use by the scientific community.

° NLM has mapped keywords in GenBank® to corresponding concepts in Medical Subject Headings (MeSH), NLM's 15,000-term vocabulary used in indexing millions of journal articles. MeSH itself has been expanded with new index terms for papers that report new biotechnology data. These two accomplishments, combined with the new workstation described above, will, for the first time, allow researchers to use one set of terms and retrieve information from multiple databases.

° The NLM is now building a "database of biotechnology databases" that will help scientists locate not only molecular biology information but also such resources as tissue banks, clone libraries, and enzyme databanks. This directory of databases will be made available in both printed and computerized form.

° The power of computer technology has made it possible to develop mathematical methods to predict the specific areas of a protein and the amino acids that are likely to elicit an immune response. This methodology has been applied by NCI scientists to the development of two vaccines. In one case, the approach was used successfully to predict the major site at which the cells of the immune system recognize one of the proteins of the malaria parasite. This protein fragment has been shown to be capable of stimulating an immune response to malaria in an animal model. Similarly, immunogenic recognition sites were identified on the envelope of the human immunodeficiency virus (HIV), the virus that causes AIDS. Using biotechnology, such protein fragments have been produced and preliminary results have shown that at least one of them can immunize mice. This new approach to vaccine development may have much to offer in the prevention of AIDS, malaria, and certain malignancies.

° The DRR provides biomaterial resources such as chromosome-specific probes and probe libraries, selected cell lines and large-scale cell production facilities to support the Nation's biotechnology research capabilities. Moreover, through its Biomedical Research Technology Program and Animal Resources Program, it currently funds nine Small Business Innovation Research grants having biotechnological relevance. Topics covered range from development of specific monoclonal antibodies and fibrous substrates for cell culture to a database management system for genetic analysis and a personal computer-based image analysis system.

° Using instrumentation purchased under the DRR Shared Instrumentation Grant Program, scientists have analyzed and compared the complete mitochondrial genomes from two species of trypanosomes. Other workers using the same instrumentation found that a clone of cDNA from a basement membrane protein in *Drosophila* has a high sequence comparability to similar proteins in mice and men. This indicates an evolutionary conservation of structure in extracellular epithelial matrix proteins.

APPENDIX C

Partial List of State-Sponsored Biotechnology Programs

1. Biotechnology Research and Development Institute, Alachua, FL

   The Institute's mission is to nurture biotechnology as a science and business by facilitating the conversion of biotechnological discoveries at the University of Florida into useful products.

2. University of Connecticut Biotechnology Center, Storrs, CT

   This biotechnology center was established in 1986 with funds from the State Center of Excellence.

3. Interdisciplinary Center for Biotechnology Research, Gainesville, FL

   This center represents a state program, associated with the University of Florida, for coordination of biotechnology research activities.

4. Office of Biotechnology, Ames, IA

   This program coordinates the development of Iowa State University biotechnology research activities throughout the relevant university schools/departments and interfaces with the activities of the Biotechnology Consortium.

5. Center for Plant Biotechnology, West Lafayette, IN

   This center coordinates the activities performed under a grant from the Indiana Corporation for Science and Technology to Purdue University for research on agricultural plant biotechnology.

6. Center for Gene Research and Biotechnology, Corvallis, OR

   This is an interdepartmental, intercollege center for collaborative research, sharing biotechnology research facilities, and fostering new funding for biotechnology research.

7. Edison Animal Biotechnology Center, Ohio University, OH

   This center is supported by the State of Ohio's Thomas Edison Program, a $233 million public/private partnership to promote technological innovation through university-industry linkages involving every major Ohio university and over 370 companies. The Biotechnology Center, which is affiliated with a "for profit" unit, Embryogen, focuses on molecular farming (i.e., the delivery of genes to animals for the production of recombinant proteins).

8. Michigan Biotechnology Institute, East Lansing, MI

   This institute, affiliated with the University of Michigan and Michigan State University, is a commercially-oriented firm devoted to biotechnology mediated production of higher value products of agricultural and forestry renewable resources.

9. Biotechnology Research and Education Program, University of California

   This biotechnology research and training program focuses on the biomedical sciences, chemical engineering, agricultural and veterinary sciences and marine sciences and involves the campuses of the University of California system and the affiliated National Laboratories.

10. Division of Biotechnology, University of Arizona, Tucson, AR

    This program provides major equipment in core user facilities, coordinates biotechnology research and education, and interfaces with industry.

11. University of Georgia Biotechnology Center, Athens, GA

    A program to facilitate university research in biotechnology, integrate interdepartmental research programs and interact with biotechnology industries.

12. Maryland Biotechnology Institute, College Park, MD

    This institute has four research centers (marine biotechnology; medical biotechnology; agricultural biotechnology; and a center for advanced research in biotechnology jointly supported by the University of Maryland, the National Bureau of Standards and Montgomery County, and a public issues program.

13. North Carolina Biotechnology Center, Research Triangle Park, NC

    This center, a locus for biotechnology interactions in North Carolina, promotes economic developments by catalyzing biotechnology research in the areas of lymphocyte technology, forestry, marine biotechnology, bioelectronics, plant molecular biology and biomaterials.

14. New Jersey Center for Advanced Biotechnology and Medicine, Piscataway, NJ

    This program focuses on basic molecular biology (structural biology, molecular genetics, cell and developmental biology, molecular virology and molecular pharmacology).

15. Cornell University Biotechnology Program, Ithaca, NY

    This program fosters biotechnology research and applications for economic development via the institute--industry consortium, the U.S. Army Center for Excellence in Biotechnology and the New York Center for Advanced Agricultural Biotechnology.

16. Penn State Biotechnology Institute, University Park, PA

    This program conducts applications-oriented research leading to new products and processes, promotes interaction with the private sector, and provides training in biotechnology research.

17. University of Wisconsin Biotechnology Center, Madison, WI

    This program provides technical resource facilities, facilitates university-industry interactions and seeks to attract relevant biotechnology companies to the state.

18. Minnesota Council on Biotechnology, St. Paul, MN

    The Council, a consortium of state government, industry, the University of Minnesota, and the Mayo Medical School, supports a program for the development and promotion of biotechnology/biomedical industries in Minnesota.

Source: Biotechnology Information Program
North Carolina Biotechnology Center
P.O. Box 13547
Research Triangle Park, NC 27709-3546

APPENDIX D

Small Business Innovation Research (SBIR) Program
Grants Funded by
the National Institute of General Medical Sciences
Fiscal Year 1987

Representative Biotechnology-Related Grants

	Biotechnology Firm	Title of Research Grant
1.	Bend Research, Inc. Bend, Oregon	Isolation of Albumin by Continuous Affinity Separation
2.	Radiation Monitoring Devices, Inc. Watertown, Massachusetts	Improved Gel Electrophoresis for Medical Research
3.	Genelabs, Inc. San Carlos, California	Rapid Approaches for Production of Genomic DNA Probes
4.	Western Research Company, Inc. Tucson, Arizona	a. CCD Digitization of Electrophoretic Gels b. A Cost Effective CCD DNA Sequence Reader
5.	Collaborative Research, Inc. Lexington, Massachusetts	Analysis of Yeast Glycosylation of a Human Glycoprotein
6.	Biosym Technologies, Inc. Rockville, Maryland	Computer-Assisted Protein Design
7.	Biotech Research Laboratories, Inc. Rockville, Maryland	Porous Microcarriers for Growing Cell Cultures
8.	Litron Laboratories, Ltd. Rochester, New York	Genetic Toxicology Testing by High Speed Flow Cytometry
9.	Applied Sciences Consultants, Inc. San Jose, California	Computer Folding of RNA Using Monte Carlo Method
10.	Biogen Research Corporation Cambridge, Massachusetts	Production of Recombinant Proteins in Milk

11. TSRL, Inc. Ann Arbor, Michigan	Technology for Oral Delivery of First-Pass Drugs
12. Synthetic Genetics, Inc. San Diego, California	New Methods for Synthesis of Fluorescent DNA
13. Biotechnology Associates, Inc. Houston, Texas	Lipid Polymer Films -- A Novel Biomaterial
14. Genex Corporation Gaithersburg, Maryland	Bacillus Hosts for Pharmaceutical Protein Secretion
15. Invitron Corporation Redwood City, California	Protease Nexin I (Mice)
16. Electrocell Buffalo, New York	Electrofusion and Electropermeation of Cells
17. Verax Corporation Labanon, New Hampshire	An Improved System for Mass Culture of Human Hybridomas
18. BTX, Inc. San Diego, California	Cell Separation in Electromagnetic Fields
19. Stratagene Cloning Systems San Diego, California	New Chromosomal Jumping Vectors for Gene Mapping
20. Molecular Probes, Inc. Eugene Oregon	Synthesis of New Fluorescent Substrates
21. Biosearch, Inc. San Rafael, California	a. A Novel Instrument and Method for Amino Acid Analysis b. Rigid Support for Solid Phase Synthesis c. Dithiasuccinoyl Methodology for Peptide Synthesis

Mr. Walgren. Thank you very much. Your full statement will appear in the record, and the text of that will be reproduced for all.

Dr. Kirschstein. Fine.

Mr. Walgren. Dr. Nelson?

STATEMENT OF DR. DAVID B. NELSON, EXECUTIVE DIRECTOR, OFFICE OF ENERGY RESEARCH, U.S. DEPARTMENT OF ENERGY

Dr. Nelson. Thank you, Mr. Chairman.

The Department was asked to focus its testimony on the genome initiative, and I will do so. I have submitted my written testimony, and so I will confine myself now to brief oral remarks.

First let me say that the Department appreciates the support that the Science, Space and Technology Committee has given to the genome initiative. Your authorization report for 1989 was very supportive. I would like to quote: "DOE was the first Federal agency to recognize the value of undertaking a large-scale research project aimed at decoding the human genome." We appreciate those kind words.

Indeed, the Department was the first to propose this initiative back in 1986, to map and ultimately sequence the human genome. We are pleased that the technical strategy that was laid out in this 1986 initiative has been endorsed by the Office of Technology Assessment, by the National Academy of Sciences, and by our own Health and Environmental Research Advisory Committee.

Some still question why DOE, why does DOE have a role in the human genome initiative? I think members of this committee understand that well but just to summarize: First, our biological and our genetic experience that grows initially out of our studies of human effects of ionizing radiation, and more recently the human insults of all sorts of environmental pollutants; and, secondly, our technical and managerial expertise in managing long-term and multidisciplinary scientific projects.

In fact, your report of this year endorsed that, pointing out, as I quote: "The historical strengths of the Department and its National Laboratories in the area of technology development and the management of multidisciplinary scientific projects make it uniquely qualified to take a leading position in the Federal genome research project." We appreciate those kind words.

I notice that you used the term "a leading position," not "the leading position," and I would certainly agree with that. Since the initial initiative in 1986, other agencies, predominantly the NIH and the NSF, have recognized the value of such a project and have begun to contribute their own expertise, their own talents and background, to this. We welcome that. We recognize the complexity and difficulty of this project, and the fact that no single agency has an arm-lock on the techniques required.

I would stress that the Department at this point does not feel it necessary or desirable that there be a lead agency, and, in particular, that the Department of Energy be the lead agency. We do believe that the Department, because of its skills and expertise, should take a leading role, just as your report has said, in some areas.

Now in order for a project like this to succeed without a lead agency, careful coordination is required, and again I quote from your report: "The committee encourages the Department to coordinate its research program with other Federal agencies funding genome research." You heard earlier from Dr. Cook-Deegan and more recently from Dr. Kirschstein about the importance of coordination and about some of the things that are being done to coordinate our programs. I would like to summarize, but very briefly because you have heard most of these already.

First, the FCCSET Subcommittee on the Human Genome meets every month to review the plans and programs, with members that include DOE, NIH, NSF, USDA, and the Howard Hughes Medical Institute. Secondly, the detailee from NIH that Dr. Kirschstein mentioned, we appreciate that. It is a human form of coordination. Third, the joint workshops that we have held with NIH and others in 1987, 1988, and more planned, are at the working level and with scientists in the field. Next, the day-to-day sort of informal coordination over the telephone and at meetings that goes on between our agencies. You have also heard about the planned meeting for international cooperation that is scheduled in Spain this fall. Finally, NIH and DOE have had discussions regarding the possibility of joint support for studies of the ethical issues associated with the genome initiative.

In addition, recently, as you heard from Dr. Kirschstein, DOE and NIH have agreed to set up a joint advisory mechanism, using overlapping members of our advisory panels, and DOE and NIH have agreed to work together and also with other interested agencies to develop a memorandum of understanding to formalize a coordinated approach. We believe that these activities and coordination, which are growing, taken together, constitute a well-coordinated but not overly hampered program.

Let me turn briefly now to comments on S. 1966, in particular provisions for the National Advisory Panel on the Human Genome. The Administration agrees with the intent of S. 1966 for a well-coordinated program, and you just heard my comments that we are carrying out this coordination. However, the Administration believes that establishing a statutory panel in this area is unwieldy. It creates a permanence and a rigidity that may be stultifying and may not allow for modifications that evolving circumstances may require. As a result, the Administration is not able to support S. 1966, as it regards the National Advisory Panel on the Human Genome.

The bad news continues. I regret that the Administration cannot support S. 1966 or H.R. 4502 with regard to the Biotechnology Policy Board or Commission. We certainly agree with the intent in both areas, the Biotechnology Board and the Human Genome Panel, but we feel that some of the duties of the Biotechnology Board and also the Genome Panel mix the policy-setting functions of Federal officials with advice from the private sector, and can lead to conflict of interest situations.

In summary, while we agree with the goals of these bills, we think that we are already carrying out in the genome initiative the provisions or the spirit of the provisions, and that the bills are unnecessary and may be detrimental to the success of this work. Our system, which has a memorandum of understanding in the genome area to provide the overall formal umbrella for coordination, the FCCSET Subcommittee, which offers the Federal coordination, and the joint advisory mechanism, which offers outside advice and policy assistance, constitutes a well-coordinated program.

Thank you for the opportunity to testify.

[The prepared statement of Dr. Nelson follows:]

Statement of David B. Nelson

Executive Director of the Office of Energy Research

U. S. Department of Energy

before the

Subcommittee on Natural Resources, Agriculture Research and Environment

and the

Subcommittee on Science, Research and Technology

of the

House Committee on Science, Space and Technology

July 14, 1988

Mr. Chairman and Members of the Subcommittees:

I am pleased to be here with you today to provide testimony regarding H.R. 4502, the Biotechnology Science Coordination and Competitiveness Act of 1988 and S. 1966, the Biotechnology Competitiveness Act of 1987. It is appropriate for the Department to comment on this legislation since the Department of Energy (DOE) supports diverse research activities related to biotechnology and the human genome initiative and the unique resources and capabilities of DOE laboratories are certain to play a key role in the development of biotechnology. We understand that the Subcommittees are particularly interested in the Department's appraisal of those portions of the legislation which deal with the human genome research project and the collection of genetic data. Before addressing that specific question, it might be useful to provide some background on the origins of the DOE Human Genome Initiative and describe some of the recent events related to this Initiative.

THE DOE HUMAN GENOME INITIATIVE: BACKGROUND

This initiative represents a new approach to a traditional DOE mission, namely, to understand the long-term health implications of energy technologies. The research proposed by the Department is a logical outgrowth of ongoing DOE research in basic and applied genetics, and in the creation of new technologies and resources for biomedical science. As such, it builds on the capabilities of the Department and its national laboratory system. Health and environmental concerns must be understood before major energy policy questions that confront the Department and the Nation can be resolved. Such concerns will have a major, perhaps deciding, influence on the mix of energy technologies with which we move into the future. The primary health-related question faced by the Department centers on the long-term impacts of low levels of radiation and energy-related chemicals.

Over the years, a variety of approaches has been used to evaluate the effects of low levels of radiation and energy-related chemicals. Each of these approaches had its limitations. At high levels of exposure to radiation and some chemicals, virtually everyone is affected; but at levels typically encountered in our daily lives, relatively few suffer health impacts, i.e., people vary in their susceptibility. One of the major causes of this individual variation in susceptibility or resistance lies in differences in genetic characteristics. Thus, the ability to characterize an individual's genetic makeup will vastly increase our capacity to identify individuals who might be particularly susceptible to low levels of toxic agents and to identify molecular changes years before diagnosable symptoms of disease appear.

It is worth noting that the technologies that will be developed in carrying out the genome initiative are highly likely to have significant application in the private sector, as was the case with DOE-funded research in nuclear medicine. An estimated 80 to 100 million nuclear medicine procedures are performed annually in the U.S.; and nuclear medicine has spawned industries valued at hundreds of millions of dollars per year. From what we know today, we believe that the technologies developed during the genome initiative will probably produce even more impressive results in the private sector. The new technologies will find broad application in nearly all areas of biotechnology, not just biomedicine, but in every application which will benefit from more efficient methods to analyze DNA from any organism.

Research which is a direct part of the current human genome initiative has been underway since 1983 when the Department initiated the National Laboratory Gene Library Project. The purpose of this ongoing DOE project is to separate human chromosomes and prepare cloned DNA fragments from each type of chromosome. The project uses the unique strengths of the Los Alamos and Livermore National Laboratories in the area of chromosome separation using flow cytometry, a Los Alamos invention. The library of cloned DNA fragments from each chromosome is a valuable research resource for the medical genetics community. The 24 libraries of clones are made available to the world scientific community through a repository funded by the National Institutes of Health (NIH).

Historically, a major thrust of DOE biological research has been the evaluation of genetic impacts of radiation and energy-related chemicals. At the Oak Ridge National Laboratory, DOE funds one of the world's largest centers for the study of mouse genetics. Over the years the Department has funded the development of a very high percentage of the biological tests used to detect somatic and heritable mutations. DOE and its predecessor agencies have funded the largest genetic study of a human population ever undertaken, the attempt to detect heritable mutations in the survivors of the atomic bombings in Japan. Efforts ongoing continuously since 1946 have found no more mutations in the offspring of the survivors of those bombings than were found in the control population. In fact, in these and other studies to date, the available methods have provided no documented evidence for the induction (by chemicals or by radiation) of heritable mutations in humans. There may, however, be subtle changes that have not yet been identified and, thus, a major emphasis of the DOE program has been the development of improved mutation test systems.

A recent (1986) report from the Office of Technology Assessment (OTA), "Technologies for Detecting Heritable Mutations in Human Beings," discussed the needs for improved technologies for mutation detection. The Report also surveyed the available methods and discussed recent advances in molecular biology which might lead to the development of such technologies for examining DNA. The report noted that "of the several funding agencies, DOE has taken the lead in funding much of the research on new methods for mutation detection described in this report, and researchers at some of DOE's National Laboratories are among the leaders in the research."

It was clear that improved mutation detection methods require much more efficient ways to characterize the molecular fine structure of DNA and to compare the DNA of offspring with their parents. It is this need for vastly improved large-scale DNA analysis and an appreciation of the many implications of such a capability that led the Department in December 1985 to organize, through the Los Alamos National Laboratory, a workshop of eminent scientists to examine the feasibility and potential utility of obtaining the complete sequence of the human genome and, if appropriate, to identify the initial steps which might be taken in effective pursuit of that goal. That workshop, held in Santa Fe in March 1986, concluded that mapping and sequencing the human genome by the end of the century is, with achievable advances in technology, technically feasible. The workshop report concluded that the effort required a central coordinating body and deserved and required multi-institutional support and cooperation, as well as a multinational constituency.

On the basis of this report, in early May 1986, DOE developed a major new initiative on mapping and sequencing the human genome. The initiative was conceived as having two phases. The first phase would have three goals: (1) the production of a physical map of the human genome in the form of ordered, cloned DNA fragments; (2) the development of high-speed, fully automated methods for sequencing DNA; and (3) the development of the computer resources necessary to organize, analyze and make available the acquired information. The second phase would concentrate on an effort focused on large-scale sequencing and would be heavily dependent on the results of the first phase.

The program was envisioned as a focused, coordinated, multidisciplinary effort to create the technologies, tools and resources which would allow much more cost-efficient studies of human biology. On May 22, 1986, the DOE Health and Environmental Research Advisory Committee (HERAC) was charged with providing advice regarding the scientific, organizational and administrative strategies for achieving the goals of the initiative. The HERAC report on the Human Genome Initiative was delivered to DOE in April 1987. Although a few projects were initiated in FY 1987, this initiative formally began this year, in FY 1988, at a level of eleven million dollars.

It is gratifying to note that the approach outlined in the DOE initiative and the HERAC report is consistent in its scientific strategy with the report, "Mapping and Sequencing the Human Genome," recently released by the National Research Council. It is also consistent with the April 1988 report of the Office of Technology Assessment, "Mapping our Genes, The Genome Projects: How Big, How Fast."

RECENT EVENTS

In approving and funding the expanded FY 1988 research program DOE has followed the recommendations of the HERAC report which stated that a panel should be established to provide scientific review of proposals and programs for their technical merit and feasibility. We received about 50 proposals in response to a notice in the Federal Register inviting applications for special research grants to support a coordinated multidisciplinary research effort aimed at creating the resources and technologies which would lead to a detailed understanding of human inheritance at the molecular level. An expert panel was convened to review these proposals for their scientific merit. About one third of the proposals reviewd by the panel received funding by DOE. As recommended by HERAC, we intend to utilize both prospective and retrospective peer reviews and to support single-investigator-initiated proposals, as well as multidisciplinary efforts involving medium-sized (3 to 10 senior investigators) research teams and a few large centers.

In September 1987, the Secretary of Energy directed Los Alamos National Laboratory and Lawrence Berkeley National Laboratory to establish centers to study the human genome. The centers will develop new technology required for the project and will carry out research on physical mapping, cloning, and eventually sequencing the human genome. The Los Alamos and Berkeley centers will have a major responsibility in coordinating efforts to transfer to the private sector the human genome results developed at all of DOE's National Laboratories. In addition, Los Alamos has been asked to explore the possibilities for cooperative research programs with the private sector to develop commercial applications of human genome research. These explorations could lead to a pilot program which might serve as a model for other DOE laboratories. Work at these centers will be established in cooperation with efforts at universities, in the private sector, and at other DOE laboratories.

COORDINATION

The Department's major role in this multiagency effort reflects the necessary combination of intellectual and physical resources that exist within DOE and its laboratories. It also reflects the Department's experience and infrastructure for handling high technology, interdisciplinary projects involving national laboratories, universities and industry. But it is also clear that a focused, coordinated, interdisciplinary effort involving the private sector, universities and national laboratories, and several modes of funding from individual investigators to interdisciplinary centers will be necessary to obtain the most efficient progress.

Coordination of all interested Federal agencies is currently being carried out by the recently formed Human Genome Subcommittee of the Committee on Life Sciences under the Federal Coordinating Council for Science, Engineering, and Technology. The Subcommittee is chaired by the Assistant Director for Life Sciences of the Office of Science and Technology Policy. Agencies represented include the National Institutes of Health, the National Science Foundation, and the Department of Agriculture, as well as the Department of Energy. The Howard Hughes Medical Institute is also represented on this Subcommittee. The Subcommittee gathers information on the relevant activities of each agency, thus helping to ensure that the research programs of each agency complement each other. It is a useful forum for the exchange of information and plans, and in which to discuss issues of joint concern to the entire research community.

Other means of coordination between DOE and NIH of activities relevant to the human genome initiative have also been established. We have jointly sponsored workshops to plan for the requirements of the project and are scheduling additional joint workshops. For instance, in May, DOE, NIH and the Howard Hughes Medical Institute jointly sponsored a workshop to discuss issues related to data management for physical mapping information, including the exchange of information between laboratories, databases for physical mapping information, and nomenclature. Our three organizations are planning additional follow-up workshops to address other data management issues whose resolution is crucial to creating a user friendly, integrated database containing all relevant genetic and other desired data. Extensive interagency cooperation is also evidenced in the operation of GenBank, the national databank of nucleic acid sequences. This databank, located at the Los Alamos National Laboratory, is primarily supported by the National Institute of General Medical Sciences, but also has support from DOE, the other NIH Institutes and from the National Science Foundation, the Department of Agriculture, and the Department of Defense.

In addition to continuous, ongoing coordination at the working level, DOE and NIH have recognized that there are scientific and other issues which are common to our programs. For the human genome initiative to proceed in the most effective manner, it would be advantageous if these common issues were addressed jointly. Consequently, DOE and NIH have begun discussions on how best to obtain such joint advice. One possibility under consideration is a joint DOE-NIH subcommittee of relevant advisory committees from each agency.

Coordination is also important at the international level. It is particularly desirable that databases and repositories be maintained so as to assure timely access to research results. There already is excellent cooperation between the United States, Europe and Japan in several aspects of this effort, including nucleic acid sequence and protein sequence databases. There is existing collaborative framework to study genetic linkage, and other nongovernmental agreements to collaborate are being established between institutions and researchers. In addition, we have had some very preliminary discussions with the representatives of other governments, particularly Japan, regarding possible joint efforts. Also, there is a meeting to be held in Spain in October to discuss international coordination of human genome research and a new international group of scientists, the Human Genome Organization, is being formed.

From the beginning, the initiative was seen as a new departure in biology. As the HERAC Report states, "This special focus on technological development is distinct from the current national effort in human biology and genetics and requires a new initiative." That sense has also been recognized in the NRC and OTA reports. All of the recent reports have discussed some of the needed new technology and noted that creation of these tools will require a broad interdisciplinary research effort that brings together expertise from a variety of fields such as engineering, electronics, optics, computing, physics, and chemistry, as well as biology. It is in the ability to bring together such diverse disciplines to focus on a coordinated, multidisciplinary effort to develop complex new technology that DOE brings considerable experience. Major technological advances are required in several areas. We need to develop automated and more effective techniques for handling, mapping, and sequencing DNA, and we need new computer data processing approaches for deciphering the messages of DNA. DOE has unparalled computer resources and expertise to apply to this effort. We look forward to working on this important and challenging project and to coordination of our efforts with NIH and other involved agencies.

COMMENTS ON H.R. 4502 AND S. 1966

Although the Administration certainly agrees with the intent of H.R. 4502 and S. 1966 to promote research and biotechnology and to enhance competitiveness of the biotechnology industry in the U. S., it does not support their enactment because they duplicate existing activities and, in fact, would hamper the conduct of research instead of facilitating it. The added layers of bureaurcracy and large panels and boards with overlapping functions as proposed by these Bills are unnecessary to improving competitiveness in biotechnology. In addition, we do not believe that establishing these advisory commissions and boards in the Executive Branch is the appropriate way to implement the goals of the legislation. Specific comments on the Bills follow.

H.R. 4502 creates a National Biotechnology Policy Commission to review Federal and private sector biotechnology activities, and to submit recommendations regarding policies which would promote research on biotechnology and enhance the competitiveness of the biotechnology industry in the United States. The Department certainly agrees with the intent of this legislation. However, the establishment in the Executive

Branch of this Commission, which includes members from outside the Federal government, mixes the policy setting responsibilities of the Executive Branch with advisory functions. Therefore, we do not believe this is the proper way to implement the goals of the legislation.

Title II, Subtitle A, of S. 1966 creates a National Biotechnology Policy Board which has functions similar to those of the Commission in H.R. 4502. As with the Commission in H.R. 4502, the Policy Board would be created within the Executive Branch and would have the same duties and functions as specified for the Commission. Subtitle B creates an advisory panel to the Board, the National Advisory Panel on the Human Genome cochaired by DOE and NIH, to coordinate national activities related to mapping the human genome by identifying optimal scientific strategies, determining goals, ensuring the quality of the work, monitoring relevant research programs, identifying commercial opportunities, overseeing interagency cooperation, assessing the need and benefit of international coordination, and evaluating patent rights and ownership of human genome data. Again, the Department agrees with the intent of Title II of S. 1966 to promote biotechnology and to coordinate national activities related to mapping and sequencing of the human genome. However, the Department, for the reasons cited above for H.R. 4502, believes that creation of a Board within the Executive Branch with membership from both inside and outside the Federal government, is not the proper way to implement the goals of the legislation. With regard to coordination of national activities aimed at mapping the human genome, as we have stated, we believe that existing arrangements have been working well. We recognize, however, that Congress desires more formal mechanisms of coordination. In that regard, we are starting to pursue with other involved agencies the development of a Memorandum of Understanding regarding coordination of activities in this area.

Let me again point out that we are in agreement with the intent of H.R. 4502 and S. 1966 and have, in fact, implemented, we believe, a coordinating mechanism to obtain the goals the legislation seeks. Establishing additional panels dilutes our efforts and makes the process less efficient.

This concludes my prepared statement. I will be happy to answer questions.

Mr. **Walgren**. Thank you, Dr. Nelson.

Where are we on this joint advisory entity that DOE mentions here?

Dr. **Nelson**. We have agreed to set it up. It is not yet set up, so watch our progress.

Mr. **Walgren**. Yes. Well, I don't know that we will have much alternative. I just—[Laughter.]

Dr. **Nelson**. I mean that sincerely, Mr. Chairman.

Mr. **Walgren**. Yes, but at this point we don't have the joint advisory board and we don't have a memorandum of understanding, and I don't have the deepest background around here but I had an awful experience with nutrition monitoring one time that was just pathetic from a bureaucratic standpoint. I can't help but be stunned by the rigidity of the turf in the various agencies that prevented them from coming to really any coordinated action, let alone a central vision.

Dr. **Kirschstein**. Mr. Chairman, may I comment?

Right from the beginning of all these endeavors, the Department of Energy and the NIH have been working together. We have attended the earliest meetings that the Department of Energy held on the genome project. They have attended our meetings, the Director's Advisory Committee meeting.

We have entered into informal agreements. For example, when it was suggested to the DOE that the type of peer review process that NIH engages in to determine what is scientifically meritorious is one that DOE should adopt, we sent Dr. Irene Ekstrand from my staff to DOE to work on that, and Dr. Smith and I talk regularly on the phone, so I think it is very different from the nutrition situation. We have been in a coordinated effort right from the beginning.

One of the reasons we do not have this joint advisory committee yet is that we are each still, or at least NIH is still working on having approval by the Department of the advisory committee that it sets up, and then appointing its own members, but we are working on this very carefully.

Dr. **Nelson**. And I would say that the DOE advisory committee will be a subcommittee of, the Health and Environmental Research Advisory Committee, which has been established for several years, so I think it is a short-term thing, Mr. Chairman. And I would point out that the genome initiative, as we have gone into the details of it, has turned out to be a very large, very diverse project.

For example, the Department of Energy continues its focus on the human genome, but you heard from Dr. Kirschstein that the other genomes of large mammals, large genomes, specifically mammalian, are of important interest as a contrast in comparison with the human genome. They range from very basic research to rather applied research and technology development.

In this case we think the Department of Energy may have greater skills in the applied research and the technology development areas, but we certainly acknowledge the skills and experience of the NIH in the basic research area. So it is really a thing that is bigger than all of us, and if any one of us tried to grab all of it or tried to exclude, and not work with our counterparts, we know it would fail. I think it may be different from nutrition, Mr. Chairman.

Mr. **Walgren**. Let me ask you, Dr. Cook-Deegan, what is your response to the concept of, "We don't want a lead agency. We pursue coordination but we don't want a lead agency."

Dr. **Cook-Deegan**. That was actually the main conclusion of the OTA report. That is one of the areas where we differed from the National Research Council. The OTA report really came out and said that a lead agency had some merit to it but probably wasn't going to work out in the long run, just for practical reasons, and that the notion of a lead agency needed to be dissected into its various components.

Let me reiterate what I started my remarks with, and that is that at the day-to-day level and at the level of operations and getting things done, there has been a lot of cooperation among the agencies. In fact, I would say for genome projects this might be better than something within the NIH or within DOE might have attained in a similar amount of time.

That doesn't address the crucial missing element, though, which is a common articulated vision. One of the nice things about being at OTA is that we are plugged into several networks simultaneously, so we hear gossip from all sorts of places, and there is a different set of people who gossip about DOE than gossip about NIH. I will say that we hear very different things from the two types of camps, and let me give you an example.

In the area of developing instrumentation or computation, this is an area where NSF and DOE have great strength and NIH has been actually moving in that direction in several areas, through the National Library of Medicine and actually also through its mainstream grant foundation, but when I talk to people who are in the business of developing instrumentation—and that will be an important part of genome projects—they just roll their eyes about what is happening in terms of coordination now, because there is no common articulated vision. It is difficult to see how that particular set of technology developments is going to be coordinated among the agencies.

Another example: In doing physical mapping, the National Laboratories have actually taken the lead, and the NIH actually has a large grant program that supports very directly related research. This is an area where there is actually some parity between NIH and DOE, therefore, but there is a different flavor in the two agencies' initiatives.

The people at DOE foresee that in the future this is going to move in the area of production work, where it does make sense for the DOE, I think, to have a big role. On the other hand, development of the new technologies to do the physical mapping, it is cloning, it is biological technologies that by and large have been developed at the NIH, and it is not clear to me how to try to coordinate something where it very clearly is going to cross departmental boundaries.

Another example is the GenBank, which is the common data source for nucleic acid sequences, that is, the A's, G's, T's, and C's that make up DNA. I think it has been a remarkable instance of interagency cooperation. There is, in fact, now an international agreement on data sharing, and it took actually 5 years of trying to gear up to—I think it now has perhaps enough resources to be successful and an advisory structure that will allow it to function.

The problem is, you don't want to go through that painful process for physical mapping, for genetic mapping, for all the data bases and resources that are going to come along the way, and I think that is what I am calling for, is some common articulated vision of what are the choke points in the future. I don't think that the very separate advisory structures for NIH and DOE, without modification, can accomplish that because, as I said, the gossip mills are separate from each other and it is in fact at that level of gossip that a lot of this coordination takes place.

Mr. **Walgren**. I see. Well, let me recognize other Members for their thoughts. Mr. Scheuer?

Mr. **Scheuer**. Thank you, Mr. Chairman.

Let me ask all of you this question. We have been informed, and actually I heard this since the testimony this morning of Dr. Merrifield, that the Office of Management and Budget and the Justice Department have some concerns about the constitutionality of this commission and they have expressed some reservations. Can you tell me how your testimony might have differed, with this whole reservation about constitutionality set aside or nonexistent? Would you have been more supportive of the idea of the commission? Is it the problems of constitutionality that may have led you to water down your support of the commission?

Dr. **Nelson**. Indeed we are aware, of course, of the Justice Department's concerns with regard to constitutionality. In my oral comments a few moments ago I didn't dwell on the constitutionality issue. In fact, I didn't even mention it. I talked about stultifying and I talked about conflict of interest.

Our experience in the Department of Energy, and I believe it is shared by the OMB, because we have indeed been talking with OMB in the course of preparing this testimony, is that when one mixes the people responsible for carrying out the law and the spending of appropriated funds with the private sector people, and certainly, in the case of the genome panel—and I think, by extension, the Biotechnology Board; although in deference I do say that my expertise is more in the genome area. I am not as familiar with the general biotechnology area. Nonetheless, the number of private sector people is about half, as I think is envisioned in both of the panels. And because the expertise in the area is fairly narrow—you can't have somebody who is working in a steel company and is an expert on the genome—there is a potential for a personal conflict of interest, a private sector person helping to formulate policy and monitor projects, as it says in the act, could be in a position of potential conflict of interest with regard to slanting things to favor his own company. I'm not saying that they will do that, but it is a potential conflict of interest. And the coordination and advisory structure that I mentioned in my comments, namely, the outside advisory committee, with, by all means, a heavy inclusion of industrial people—because we in the Department of Energy are as concerned about moving these research results into the commercial sector as I think you are, Mr. Scheuer—the outside advisory committee, FCCSET, the Federal Coordinating Council on Science, Engineering and Technology—under OSTP, provides a way for the Feds to get together, we think, while avoiding the conflict of interest.

As a result, sir, even without the constitutionality issue, we would not support these bills.

Mr. **Scheuer**. Now, why would you not support an action for a constitutionality issue?

Dr. **Nelson**. Because of the conflict of interest and the stultifying effect of it.

Mr. **Scheuer**. All right. Now, the conflict of interest comes, according to you, from the monitoring—the function of monitoring individual projects. Do you think it would help alleviate your concerns if we excluded the private groups from monitoring projects, but just got their involvement in the public policy questions that our country has to address?

Dr. **Nelson**. I believe it would go a long way. I'm not prepared to say at this point what provisions of a bill would make it acceptable to the Administration, but by having already said that we support the intent of the bill, there may indeed be a way of reaching a commonality.

Mr. **Scheuer**. Dr. Kirschstein?

Dr. **Kirschstein**. Yes, it is the position of the Department of Health and Human Services that the reasons for opposition to this bill are related, as Mr. Nelson said, to the fact that we support the intent and the goals but do not feel that this formal mechanism is needed to assure the cooperation and coordination that we feel is already going on.

The issue relating to constitutionality is something that was raised with us very late yesterday afternoon, and as you will see from my written statement, it was placed in the statement; but I would not have any comment on it, and I don't think that would have changed my testimony.

Mr. **Scheuer**. Dr. Kirschstein, let's leave aside the question of constitutionality. Maybe by jiggering it and excluding the private interest representatives from the monitoring function, restricting them to discussions of general public policy, let's assume we can solve that problem.

You heard a great deal of testimony this morning from Dr. Kathi Hanna about the inadequacy of the present level of interagency cooperation, large gaps. You heard testimony about the desirability of further collaboration and "brain-trusting," so to speak, of these many complicated questions of public policy that would benefit from some kind of mutual intellectual brain-sharing between the public and private sectors. If we could eliminate the problem of constitutionality by one means or another, perhaps by, as I say, excluding the private sector representatives from the screening and oversight of individual projects, don't you think there is room for the kind of collaboration—more collaboration and more coordination between the agencies, the need for which has been amply discussed this morning? I mean, what you're saying is that the present situation is hunky-dory and we don't need to enhance interagency cooperation——

Dr. **Kirschstein**. No, Mr. Scheuer.

Mr. SCHEUER [continuing]. And there's no reason for us to seek the involvement of private sector people on these important public policy questions?

Dr. KIRSCHSTEIN. I'm not in a position of telling you whether by leaving that one part aside, the Administration would change its position on the bill. I would say that I do totally support the intent of increased and enhanced coordination in every way, and I would feel that we need to do that whether we do it formally or informally. I would also pledge to you that if by chance there were no formal mechanisms, I as the chairman of the NIH Biotechnology Activities Committee will see to it that we work very hard to enhance such coordination.

Mr. SCHEUER. Well, thank you very much, Dr. Kirschstein. I welcome that initiative and that assurance.

I have to footnote it by saying that we have a Government of laws, not of men or women, and probably we ought to seek to find an answer to this institutional problem so that there can be direct, official collaboration.

Dr. Cook-Deegan, do you have any observations on this question?

Dr. COOK-DEEGAN. I'll go back to my main point. I think that raising the issue of constitutionality and all that is, frankly, a little absurd. It could be that——

Mr. SCHEUER. Do you mind if I interrupt you there?

Dr. COOK-DEEGAN. Sure.

Mr. SCHEUER. I think it's not a little absurd; I think it's grossly, totally, offensively absurd. [Laughter.]

A great English legal commentator said in the last century, "The law is not an ass." [Laughter.]

Now, I wouldn't use language like that if a far greater legal mind than mine hadn't given it to us a century ago. "The law is not an ass," he said. What I would say is that the Constitution isn't an ass, and Government is not an ass. And in this day and age if we can't find an institutional format for collaboration between Government and industry on this incredibly complicated and sophisticated and very important question of biotechnology, how we organize our effort, to what extent it is appropriate to guide it, to what extent it is appropriate to set priorities, then there is really something rotten in Denmark. I can't believe that we're so stupid that we can't find an answer to whatever constitutional concerns might be raised, and perhaps properly raised.

I call to your attention that we have had several commissions like this. The Rogers Commission, which was set up after the Challenger accident, involved public and private representatives on an individual failure involving individual Government contractors. The Roddis Commission, involving nuclear waste, also involved public and private representatives on that commission. I believe that if we asked the Library of Congress to give us an historical look at this matter, we would find an infinity of examples where we have managed to create Government institutions where public and private interests could collaborate.

You know, one of the problems that we have had in our society that has created enormous problems is that Government goes this way, and private industry goes that way. We have problems of acid rain; we have problems with ozone; problems of nuclear warming, and then because of the lack of collaboration at a very early point, now we are faced with enormous problems with enormously costly and time-consuming remediation needs, and sort of a built-in confrontation where the chemical industry is hiring $300-an-hour lawyers to fight the regulations that the EPA is proposing to regulate toxic wastes and regulate acid rain and so forth.

I mean, give me a break. Is that constructive? It seems to me we ought to be searching, and the OMB should be searching, for ways of getting intelligence-sharing, experience-sharing, collaborative efforts to avoid these awful problems early on in the game. I just can't believe that in July of 1988, it's rational, and not terribly counterproductive for the OMB to tell us that we can't have joint collaboration between Government and industry to find better solutions, better coordination, better concepts of funding, better concepts of priority-setting than we have now. I just can't believe that, as intelligent human beings, we can't solve whatever technical constitutional problems are there by means of, perhaps, altering this formula. God didn't hand this formula down to the commission along with the Ten Commandments. We devised it, and what we devised we can change. We can massage the language. It just defies my understanding for any responsible Government agency to say "no" on the concept because there's a technical problem. Let's get together and solve the technical problem of constitutionality, if there is one.

Yes?

Dr. NELSON. Could I comment?

We've heard this morning about the Japanese competition; also, of course, the European, but I'd like to focus on the Japanese as an alternative—which I don't agree with, by the way, because I don't think it maps to our country.

Mr. SCHEUER. You don't believe what?

Dr. NELSON. I don't believe that the Japanese mode of coordination "maps" well. It doesn't agree with the history of our country. If you look——

Mr. SCHEUER. Well, we know that the result of the Japanese formula is very threatening to our country. If we can't achieve something like that result, maybe by jiggling or massaging the technical means to achieve that degree of priority-setting and coordination and funding, we're going to be in very sorry shape, because following their success in wiping us out of international global competition in computer chips and robotics, they're going to wipe us out of the field of biotechnology. And you heard the Japanese—this distinguished Japanese-American expert, Dr. Akihiro Yoshikawa, talking about "us" and "our." He's an American; he's a Japanese, but he's an American citizen and concerned with our country. He certainly sent up an early warning signal that we would ignore at our peril.

We have got to find answers to these problems.

Dr. NELSON. In Japan, though, they have a tradition of sitting down in a room, maybe over several days or even months, but carving up the pie in a mutually acceptable fashion. Now, in this country that doesn't seem to have worked so well because the people who aren't in the room object to those who were in the room.

I think some of the testimony that we heard this morning in earlier panels—you probably heard some reservations with regard to whether a monolith, and a panel or board can become a monolith, would survive the scrutiny of those who aren't on it.

I certainly agree with you that we're in a real bind and we have to find better ways of working together. I would just venture that trying to import the Japanese model may not work in our culture.

Mr. SCHEUER. I quite agree with you, that we cannot just lift a pattern that is rooted in Japanese history and culture and traditions and mores and apply it indiscriminately to our country. That makes sense; nobody is suggesting that. But as to the success of their system for allocating resources, for amassing and directing capital at important national goals that have been developed through consultations between business and industry and between important business institutions, I can tell you that we've got to find a way of doing that in a means that is consistent with our traditions. We have got to do it.

The question may not be—let's talk about the antitrust implications. The question may not be whether we have got to preserve four automobile companies, three biggies and a somewhat smaller one. The question may be, if we don't get our act together, is there going to be a single automobile company that is going to survive in this country once the Japanese have produced their cars that get 80, 90, 100 miles per gallon?

It may be that we've got to pool our resources and achieve ways of defining national goals and aggregating the capital, both cheap capital and patient capital that will help the automobile companies working together, all four of them, to produce a car for the year 2000 that will be an effective competitor in global commerce. Otherwise, all four of them may go the way of the blunderbuss, of the dinosaur.

This is a matter of national economic survival, and we'd better come up with solutions. If there is a constitutional problem, and maybe there is, we had better analyze it and come up with formulas for avoiding the constitutional problem but achieving these goals. You can't just say, "We approve of the intent, but since there's a constitutional problem, we're not going to be able to do that." We've got to do this.

Mr. Walgren?

Mr. WALGREN. I yield my time, Mr. Chairman.

Mr. SCHEUER. The Chair recognizes the gentlewoman from Maryland, Mrs. Morella.

Mrs. MORELLA. Thank you, Mr. Chairman.

It was about 10 years ago, maybe a little longer, that I was teaching at Montgomery College. One of the books I taught in terms of scientific revolution was "Brave New World"; that was written by Aldous Huxley in 1932. In it he had the various classes, the alphabetas, the gamma-deltas, the epsilons, and at that point genetics wasn't even talked about. Now, when you talk about future shock, in that 10-year period where biotechnology has come—here we are, talking about mapping the human genome. It's really incredible.

Incidentally, yesterday—I guess it was yesterday; I lose track of days—Congressman Scheuer was involved in chairing a conference on biotechnology. I had an opportunity to make some comments, and naturally, I talked about the district that I represent, which is the core of the greatest biotechnology capital of the Nation. Much of that has to do with its proximity not only to the Washington area, but to the National Institutes of Health, for what it has done, and I think it has 10 percent of the Nation's biotechnology companies. That's all in the way of congratulating all of you who are involved and interested in biotechnology, in continuing what you're doing.

Now we're talking about mapping the human genome and the problem of whether or not there should be some kind of legislative coordination, and I'm wondering, just from the little bit I know, it seems as though—we talked about international competition, but there doesn't seem to be that much international competition for that part of the work, the mapping of the human genome. I'm wondering if, because you might be allowed to proceed a little bit slower because maybe there isn't as much international competition, that you might want to comment on whether you could focus to begin with on human defects and how that would work out. I say that because I understand that to really accomplish what you want to would cost multi-billions of dollars, so one of my questions would be the money part of it; and secondly, could you not tend to concentrate on human defects because you might have the luxury of a little bit more time? Thirdly, what is international competition like, and what is international cooperation like?

That's a lot, but I would just like to have each of you comment on any part of that.

Dr. KIRSCHSTEIN. Perhaps I could start.

The efforts that NIH over the past 20 to 30 years has made, culminating in fiscal year 1987 in spending approximately $365 million, have been specifically looking toward identifying the genes of interest that have been responsible for the defects. And it's really quite remarkable, what has happened. We have mapped—that means, we have found the approximate location in the last several years—the genes for Huntington's disease; Duschesne's muscular dystrophy; retinoblastoma, which is a cancer of the eye in children; some forms of manic-depressive illness; cystic fibrosis; cancer of the colon; color blindness; Alzheimer's Disease, and there are many more.

As we are beginning to identify more and more of those specific genes, the idea of the human genome project has become more important because what has been realized is that between those specific genes that are located throughout our chromosomes and that specify particular defects or diseases, there is a vast amount of genetic material, nucleic acids, DNA, which must be identified so that we can put all those genes in the right location and understand how they work, because the material around them settles how they regulate themselves, why they may be missing or defective, how they will be allowed to be corrected. So we have to have these two projects moving simultaneously. We have for many years been moving toward this one that you're talking about, and now we feel that in some ways we have to start the next project.

Now, you had mentioned that spending a great deal of money for this new genome project is what is planned. We are planning that, all of us, in a very phased process. The Congress appropriated $17 million to NIH in fiscal year 1988, and I believe it was $12 million to DOE. In 1989, the President's budget for NIH is $28 million, and I believe that for DOE it is $18 million. I don't think anybody is proposing to start this as an enormous project, but to gradually build up. The National Academy of Sciences suggested that the appropriate level of funding in five years would be about $200 million. That is not to say we would not go on looking for these specific genes that are causing specific diseases, and beginning to try to do something about them.

The progress has been enormous. We are only just beginning.

Mrs. **Morella**. Do you feel that level of funding, on the point that Dr. Cook-Deegan made, is adequate to continue with what you are doing?

Dr. **Kirschstein**. Yes. And we think it would also be very important not to have either one of these efforts be to the detriment of the other, that the basic research and the applicability of finding the specific genes for diseases that are so devastating to so many of our population would be very important; and at the same time, this measured response of beginning to fill in the gap.

Dr. **Nelson**. Let me comment. You have three questions. I agree entirely with my colleague, Dr. Kirschstein; I just have a slightly different perspective.

Your question with regard to the money—the way genes are currently mapped or sequenced is really a cottage industry, a few thousand bases at a time. We've got about three billion base pairs in the human genome, and we can't get to anything approaching that level of sequencing without at least a ten-fold reduction in the cost, from about a dollar a base down to at least ten cents a base.

Now, this means that money spent in developing technology will have a big impact on reducing the cost. As Dr. Kirschstein said, nobody is talking about "brute force techniques" for sequencing the human genome that would add up to multi-billions of dollars; it's just not appropriate. But I would point out that once this technology is developed, it is available for studying the defects in human genes that you referred to. One speaks of "the human genome" but we're all a little bit different. So initially one might take a person or a set of people, but ultimately what we want to do is to understand how these genes—these bases—affect our makeup, so we'll want to look at variations away from a standard.

The same technology that allows us to define the standard will allow us to study the variations, to look at the precise defects that cause the diseases that you referred to.

So it is a multi-pronged thing, as Dr. Kirschstein mentioned.

I would comment last on your third question, international cooperation versus competition. I'm afraid I can't agree that we're in a relaxed mode with regard to international competition in this area. I think we're ahead. When we started this in 1985 it was built on a sound base of biotechnology in this country, stretching back, as Dr. Kirschstein said, at least 40 years. We were the first country to really say, 'Let's do this," and I think we still have perhaps a two- or three-year lead. But, you know, that can be erased very quickly.

I believe that we should cooperate: cooperate in the data, cooperate in some of the basics of possible techniques. But I believe we should compete when it come to patents; in some cases, to commercial data; and certainly, in the development of products. Not just chemicals, not just drugs, but machines as well, like some of the diagnostic machines used for actually determining the specific bases in a defect. And I don't believe that we can afford to rest on our laurels.

I think, as Mr. Scheuer mentioned earlier, it is important to get the results of this research—some of it is applied research and technology development—into the American private sector quickly. I know that in the Department of Energy, to tell it truthfully, we have changed our stripes over the last five to ten years. We are pushing technology out as quickly as we can, with a due understanding of the value of scientific data and the openness of scientific research.

So we need to both cooperate and compete.

Mrs. **Morella**. If you were to look at what country you think might catch up within that two-year lead that we have, would it be Japan?

Dr. **Nelson**. I think it could be either Japan or countries in western Europe. But I tell you, I am not sufficiently expert on the detailed state of the research of those countries to be authoritative on that.

Mr. **Scheuer**. Will my colleague yield on that?

Mrs. **Morella**. Yes, indeed.

Mr. **Scheuer**. Dr. Yoshikawa told us just a few minutes ago that when he was back in Japan, perhaps three years ago, they had no machines in this area; and now, he says their labs are full of the machines that they have developed themselves. So there is a very critical time frame here that we fail to address at our peril, it seems to me.

Mrs. **Morella**. Thank you.

Dr. **Kirschstein**. If I could just make a couple of comments here——

Mr. **Scheuer**. Dr. Cook-Deegan, I'm afraid I interrupted you before when you said this seems a little absurd, so I apologize. [Laughter.]

In your remarks, when you finish what you were going to say on that, if you could just take off on that subject?

Dr. **Cook-Deegan**. You gave me the luxury of not having to say anything, and saying it more strongly than I would have said it. [Laughter.]

In fact, I will answer that question right now and then I'll go to your questions, Representative Morella.

First of all, I was just going to say that perhaps what OMB is worried about is that there are two ways of thinking about what this advisory committee might do. One is that scientists would be coming in, telling the agencies how to spend their money and how to formulate their budget. I don't think that's what anybody has in mind. I think what they have in mind is a place where the goals of the human genome project could be articulated, in the case of the genome panel, and biotechnology policy could be articulated in the case of biotechnology, rather than saying, "You're going to spend this much on this program." That, everybody would agree, is absurd; to tell NIH and DOE how much money to spend on which programs is not for an outside committee to do. On the other hand, it is for an outside committee to be able to do what NIH and DOE cannot do, which is come up with a joint strategy.

In connection with a couple of your questions, the disease-oriented research is in fact already much, much larger as a proportion of funding than the genome projects. The thing that's unusual about the genome project—in fact, the whole idea—is to create technologies and common resources to make that sort of research faster. So that was the whole logic behind coming up with the idea of the human genome project.

In Dr. Kirschstein's written testimony she had some numbers that she didn't have time to talk about. They already spend $400 million a year doing that sort of research now as compared to the $28 million that is asked for the genome project specifically, so it's actually a much larger effort for that sort of targeted research.

On the international aspects, I have a couple of observations. One is that there is a balance between scientific cooperation and technological competition, and they are two different sets of issues. Yet, genome projects do bridge them; they have little pieces that relate to all of them.

In the area of international scientific cooperation, I think there's a wonderful opportunity here. What other nations have been doing—it may seem like they're kind of dragging their feet. In fact, what I think has been happening is that the other countries are waiting to see what the United States does because we do such a high proportion of funding of the fundamental biomedical research. They've been kind of waiting to see what the big guy on the block does so that they can decide what they're going to do.

Since this year's budget request went in, France and Italy have both dedicated funding for genome projects. Japan has had projects underway since 1981 in the area, and the European Economic Community is seriously discussing putting some money into genome projects. So it's something where there is mounting enthusiasm, and I think what you're seeing is just a result of planning going on in the United States now.

I think there is widespread agreement among scientists that there are certain things that need to be shared. There are very clear areas; for example, data—you don't want one country to have a lock on sequence data. In fact, it just doesn't make any sense to try to have a gene's location known by one country and not by another. It's against the norms of scientific discourse. So there is agreement at that level that the data bases should be shared internationally; that is, the fundamental scientific research and the basic core data should be shared. There are mechanisms for trying to do that, and I think it's a wonderful opportunity for internationalizing that process more than has been done in the past in biology.

On the other hand, at the other end of genome projects, there is this component that says, "We're going to develop new instruments for analyzing DNA, for automating current processes." There is undoubtedly going to be international competition in that area, and there should be. In those areas I think it's going to require a different set of policies in the United States, because you don't want to be exporting patentable inventions. You want to be thinking about intellectual property protections. When you're sharing information, where do you draw the line when you're sharing an invention?

There are lots of rather broad gray zones that need to be thought about very carefully, and that's why I think some strategic——

Mrs. MORELLA. If I might interrupt you for a moment.

Dr. COOK-DEEGAN. Sure.

Mrs. MORELLA. Are the legislative mechanisms in order for that kind of thing to happen?

Dr. COOK-DEEGAN. I think that it's not even a legislative issue right now. I think it's a set of issues that haven't been completely thought through by anybody, because the technologies are moving very rapidly and it's something that's going to have to be solved along the way. That's why I think it is important to have a place where all this information funnels to, and then they can decide which of these is a patent issue and which isn't, what we are and are not going to share, and that needs to involve both national level and international level decision-making. So they need to be integrated, those two processes. I hope that helps.

Mr. SCHEUER. Of course, Dr. Cook-Deegan, it is precisely to face up to those questions, inter alia, those very perplexing questions in which there has to be wisdom-pooling, experience-pooling between the public and the private sector, that we've set up this commission. I couldn't agree more with everything you've said.

And you too, Dr. Kirschstein, and all of you.

Dr. KIRSCHSTEIN. May I add something, sir?

In terms of the data, right from the beginning, which was about 1982, as we began to collect nucleic acid sequence data, the genetic banks were set up internationally. The European Molecular Biology Laboratory and the NIH were sharing in putting the information into the banks. Half of it was being done by the Europeans and half by the people in the United States.

Just recently, maybe six or eight months ago, there has been established the DNA data base of Japan, and those people have now met with us and we have formed—on an informal basis, but nevertheless working very well—a three-group advisory committee. We will meet in the United States; we will meet in Heidelberg; we will meet in Japan, and we will now have a three-way sharing of the entry of the data. There is excellent international cooperation in this regard.

Mrs. MORELLA. Thank you.

Thank you, Mr. Chairman.

Mr. SCHEUER. Thank you, Congresswoman Morella.

This whole question of what we hoard and what we share is enormously complicated and a terribly important question that we're not going to settle in the course of this hearing, and that will be one of the major roles of the commission, to sort of parse out. But can any of you describe some of the places where we might draw the line? For example, can we do joint projects with the Europeans and with the Japanese on basic research and then say, "All right, when it comes to applications, we're all going to share in this pool, and that's where the competition is going to be"?

I say this because this isn't a technology for just producing a better car or a better mousetrap or a better squawk-box, a better consumer electronic product. A lot of these applications of biotechnology in the field of health and the improvement of agricultural products of all kinds will produce enormous benefits in the third world; crops, for example, that will withstand drought and insects, that will require less irrigation, less fertilization. I mean, there's a real global public interest in getting this stuff out there and in use. It's not just purely a private enterprise business. It matters little whether the latest VCR comes sooner or later. Over the fullness of time, mankind will not measure that as very important. But whether we develop some of these new plant and animal species and some of these new health applications is of considerable importance to mankind and will save, perhaps, millions of lives and enhance the quality of life, especially for people in the developing world if we can get this basic information—this basic, pure research—out there, and then let the competition be on applications.

Does this make sense? Is there any other formula that you would devise that would provide a rational program of where there should be data-hoarding—first, let's say where there should be data-sharing and joint involvement, and at what point we say, okay, we've done the basic research, now get on with it and let's have the competition on the applications? Is there a better way of parsing it out?

There ought to be a way of saving time, and therefore saving lives, and improving the quality of life in all of these areas for peoples around the world. The Japanese have a lot to contribute to us. The Europeans have a lot to contribute to us. We probably are still first, although that lead may be faltering somewhat. We have an enormous amount to contribute. Isn't this a case where, at least for basic research, the whole is greater than the sum of the parts? We ought to find mechanisms for collaborating and then say, all right, this is for applications, machines, tools, get on with it and do your thing?

Mr. NELSON. I certainly agree with you. I would add, though, that this is complex. I realize——

Mr. SCHEUER. Of course it's complex.

Dr. NELSON. But let me give you a specific example of the complexity.

Dr. Merrifield testified earlier about the Superconductivity Competitiveness Act that the Administration has introduced. One of the provisions of that act is a modification of the Freedom of Information Act, FOIA. You might ask, what do those have to do with each other? But the answer is that if we do joint work—for example, in our National Laboratories—between Government funding and private funding, the data that results from that joint work—and in the case of industry funding, it may be leading to what they would want to have as proprietary data, because it leads to a product—that data may be releasable. We don't know, but we think that it may be releasable under an FOIA request.

Now, FOIA is an important part of our laws. It has safeguarded the openness of our political or governmental system. But here is an application of FOIA that may frustrate efforts for private sector and Government funding to work together toward near-term commercialization, where proprietary data could be an important product.

This is just one example of the complexity of determining where the proper boundary is between openness—which is for all, but for no one in particular--and closedness which leads to commercialization, because I have something that I can sell; I own it and you don't.

Mr. Scheuer. I totally respect that dilemma that you've given us. That is a conundrum of massive proportions.

Dr. Nelson. You'll have to deal with it because I believe the bill has been introduced, so Congress will have to take up this question of modifying FOIA.

Mr. Scheuer. Of course, we have to deal with it.

Dr. Cook-Deegan. I had just a quick comment. I think——

Mr. Scheuer. Well, wait a minute, let me just finish here.

Dr. Cook-Deegan. Sure. I'm sorry.

Mr. Scheuer. What I'm suggesting is that there ought to be a way of investing real resources, and maybe this is the part where the Government does funding for the fundamental research, and then turns the private sector loose. When I say "Government," I mean all these governments.

There is talk about burden-sharing in terms of our military defense. The Japanese are spending no more than one percent of their GNP; it's a constitutional limitation that we provided them gratis, coming from our own Government right after the end of the war. We spend 6.5 percent, so there has been talk about burden-sharing.

Isn't this a way that there could be some burden-sharing? Perhaps we could suggest to the Japanese that there would be an asymmetrical contribution to a joint fund for basic research, part of which they would consider their contribution to burden-sharing. After all, a lot of these new developments are going to be of enormous benefit to the third world in a whole variety of ways. This could be their form of burden-sharing; and we would contribute something, perhaps asymmetrically, and the Europeans would, too. Then when it got to the point of applications, then the collaboration would end and private competition would commence.

Is that a conceivable formula?

[No response.]

Mr. Scheuer. Who knows? We have to discuss it.

Excuse me, Dr. Cook-Deegan?

Dr. Cook-Deegan. You're asking whether there's a way that you can determine what should be shared and what shouldn't, and there's a short answer but it's difficult to figure out what it means. That would be that you share data, and you keep your intellectual property rights to inventions. That would mean that you file patents on things that are patentable, and you share everything else.

Mr. Scheuer. Would some of that basic research have a proprietary characteristic to it?

Dr. Cook-Deegan. Yes, it will, but as of right now there are laws in place that say that if a scientist has something that's supported by Federal funds—if they develop it using Federal funds—then they are obligated to notify the agency that is sponsoring their work that they are either going to patent it themselves or give the Government the right to go ahead and patent it.

Those are relatively new laws. The regs (regulations) just came out on them last April. These are areas where there are actually policies in place; they just need to be abided by. I think that scientists need to think about that as they are structuring their scientific efforts.

But I think that's a short answer. Share what you can and make sure that along the way, before you make stuff internationally available, you file your patents.

Mr. **Scheuer**. Yes, and I guess all countries have to have a concern of preserving and protecting what is legitimately proprietary information. The question is, where do you draw the line?

Dr. Kirschstein?

Dr. **Kirschstein**. No, I was simply going to add that, yes, scientists are being encouraged now to patent their basic research; indeed, because of the great interest in biotechnology, the NIH is setting up an Office of Invention Development. The new Federal Technology Transfer Act provides for the returns or royalties on patents to be shared by both the scientist, the laboratory, and the institution in which he or she works, and the other organizations. This year NIH has had a return from what its scientists have patented in royalties of over $4 million.

Mr. **Scheuer**. Well, when you're talking about a business that's going to approach $100 billion by the end of the decade, that $4 million is modest.

Dr. **Kirschstein**. That's right. We're just starting and just evolving.

Mr. **Scheuer**. When talking of an investment of $2.7 billion, it's modest. It's almost inconsequential.

One of the fascinating things about being a Congressman or a scientist or a Government administrator in this whole field is that biotechnology has sort of burst upon us with potential for human betterment that is absolutely awesome and humbling, and it well behooves us to think about how we can aid and abet this process which has such an incredible potential for improving the human condition and reserving that which is Caesar's to Caesar, but that which is God's to God.

There has to be a way of speeding up the process and sharing talent and expertise and knowledge among the great industrialized nations of the world, to speed up this whole process for the enormous benefit of the global population, and also at the same time preserving the incentives and the free enterprise system that do trigger the engines of development. There's got to be a way of harmonizing the need for joint effort, joint talent-sharing globally, to save time, to get the knowledge out there that is going to spawn the applications that have such incredible, unbelievable, unimaginable potential for improving the human condition.

Dr. **Kirschstein**. May I add one more thing, Mr. Scheuer?

Mr. **Scheuer**. Yes, of course.

Dr. **Kirschstein**. The one thing we must not forget along the way in this is the enormous shortage that we are facing of well-trained, creative minds. We have got to do something about that, as well.

Mr. **Scheuer**. I couldn't agree more. That's a major part of the problem at the Patent and Trademark Office. I mean, if you ever had an example of "for the want of a shoe, the war was lost," or "the empire was lost," for the want of a few hundred professional people in the field of biogenetics to massage these applications—for the want of them we've got a two-year waiting list holding up approximately 7,000 applications, and really presenting a potential for crippling the entire American biogenetics industry. If ever there was an example of, as I said, "for the want of a nail, the empire was lost," that's it.

The need for well-trained scientific personnel in this area is awesome, and we cannot avoid it. We've got to get on with it. This next Administration in Washington, of whatever party—it doesn't make any difference—they have to bite the bullet and say, look, we've got to reduce the budget and get our economic act together in the short term, but while we're doing that we have to think about the long term too, and these are absolutely necessary investments that must be made to preserve our competitive posture in this rapidly-emerging field that has such an incredible and dynamic impact on our economy and potential for bettering the human condition, as I said before.

So I couldn't agree with you more on the question of trained manpower in this field. It's absolutely one that we must urgently address.

Any closing remarks by any of the three of you?

[No response.]

Mr. SCHEUER. Well, it's been a fascinating panel, and I thank you all. It's been absolutely remarkable, and we'll probably be back to you with some questions. Thank you so much.

Now we will get on to Panel 3: Richard Godown, Industrial Biotechnology Association; Dr. Bruce Mackler, Association of Biotechnology Companies; Anne Hollander, Conservation Foundation; and Dr. Ralph Hardy, Boyce-Thompson Institute for Plant Sciences at Cornell University and BioTechnica International.

First, let me express my deep appreciation to all of you for hanging in here. It's been almost five hours since this hearing started, but I think you sense our feeling of excitement and great anticipation of what's going to emerge from these discussions and the whole field of biotechnology. Everybody who gets into this field of biotechnology seems to get caught up in the incredible implications and possibilities of this field. So if some of those panels dragged out and delayed your lunch, we do apologize.

We do have a press conference scheduled in this room for 2:30, but we've changed that; now we're free. Having due regard for the golden rule that "the mind cannot absorb what the seat cannot endure," we'll hang in here and take great pleasure in hearing from these four marvelous witnesses, most of whom we had the pleasure of hearing from two days ago at our wonderful all-day session on biotechnology, chaired by the Congressional Clearinghouse on the Future.

So we will recognize you all for seven or eight minutes. We're not going to be strict if you go over by a minute or two. We will take you in reverse order so that we get the public interest point of view firmly expressed, and then we hope that Dr. Mackler and Dr. Godown can sort of respond. We are keenly looking forward to this great panel.

So let's start with Dr. Ralph Hardy, and I hope that all of you—as I said before, your prepared remarks will be printed in their entirety in the record, and I hope that all of you can just address us informally and chat as if we were together in the living room.

Dr. Hardy?

STATEMENT OF DR. RALPH W.F. HARDY, BOYCE-THOMPSON INSTITUTE FOR PLANT SCIENCES, CORNELL UNIVERSITY, AND BIOTECHNICA INTERNATIONAL, INC.

Dr. Hardy. Thank you, Mr. Chairman, Congresswoman Morella. It's certainly a pleasure to participate in this hearing on biotechnology and biotechnology competitiveness. I'd certainly agree that this is a very exciting area, and as I indicated a couple of days ago at the Clearinghouse meeting, it's one that I'm extremely bullish on.

I wear a couple of hats; in a sense, I represent both the public and the private sector. I'm the president of a small institute formed about 64 years ago called the Boyce-Thompson Institute that focuses on plant sciences. It's the institute that did the fundamental science that led to the discovery of 2,4-D in the 1940's and the use of that compound for more than 40 years as a herbicide. It's an institute that now is focused on plants and food and the environment and biological control of pests, and has the only major ongoing study in the world at this time in terms of seeking a definitive answer to the effects of acid rain on forest decline.

Also, I was President and am now Deputy Chairman of a small development-stage biotechnology company called BioTechnica International Company, located in Massachusetts with subsidiaries in the United Kingdom, Canada, and the Midwest——

Mr. Scheuer. Dr. Hardy, before you get on with the substance of your remarks let me just add that in testifying—this is for the four of you—don't limit yourself to your own prepared testimony. Please feel free to address any of the colloquy that you've heard here this morning, any of these important policy issues. Sort of liberate yourselves and go where you think the important public policy questions are. How do we guide this industry as it emerges? Where do we provide Government financing? Where is it appropriate and necessary? What are the criteria for goal-setting? How do we sort of liberate this great beast that's emerging?

Dr. Hardy. Very good. I appreciate your willingness toward liberalizing this.

Let me then focus on the agricultural biotechnology area, and let me focus on competitiveness in that area. There are three points that I would really like to leave with you.

The most important point from a Government point of view in agricultural biotechnology and competitiveness is a need for an expanded quantity and quality of molecular and ecological/biological research knowledge. That is needed for the development of agricultural products and it's needed for efficacy in their use and safety. That's the most important thing we need on the agricultural biotechnology side from Government at this stage.

The second most important thing that we need is the availability of financing at favorable terms. This, of course, has been mentioned earlier today.

The third thing is a regulatory environment that is realistic.

Let me address the need for investment dollars under favorable conditions. We do have in agricultural biotechnology at this stage a commercialization structure that is being put in place. We have a healthy mix of large, established development-stage companies; they've got a critical mass of science, technology, development people with commercialization experience focused on agriculture, but interestingly enough, with more product and market diversity than the health care companies have at this stage. The agricultural biotechnology leaders are emerging in this area. We might identify five from large companies that I think are emerging as leaders, and possibly five from small companies that are emerging as leaders. Their commercialization plans are being defined and beginning to be implemented. They are a few years behind the health care industry.

Costs will be greater per product in this area than they have traditionally been in the agricultural area. Where it might take a couple of million dollars, in fact, to develop a new corn hybrid using traditional technology, it may in fact take $10 million to develop a corn by genetic engineering which will have considerably more value in use, but obviously much more investment in it at the time that it is introduced into the market.

The bottom line, then, is that if we are going to sustain and encourage this rich structure we have developing in companies to commercialize agricultural biotechnology, we're going to need a favorable investment environment for both the agriculture R&D and also for the manufacturing aspects. That's point one I'd like to make.

The second point I'd like to make has to do with the regulatory environment. It's encouraging, I think, that field research is progressing in the agricultural area. Between 1986 and 1988 we've been able to take plants with herbicide resistance, insect resistance, disease resistance, microbes with the potential for cold tolerance, insect pest control, and increased productivity into the field for the first try.

A number of reports have come out, including the OTA report, suggesting minimal risk. A report put out by the institution with which I'm associated, Boyce-Thompson Institute, looked at regulatory considerations in genetically engineered plants, looking at the agricultural and environmental risks—this was a highly focused meeting on the major U.S. crops. It came to the conclusion that there is negligible risk for most major U.S. crops, genetically engineered with near-term changes, introduced into the U.S. environment for testing, and also for commercial use. A copy of that report is available if you would like to have that.

We are now in the process of focusing on the food and feed risk area, and late this year or early next year we will bring together a broad mix of people with relevant skills in that area to identify what risks are associated with genetically engineered crops, genetically engineered plants, being used as foods or feeds.

There were some recommendations that came out of this meeting that I've mentioned that I'd like to note. It would seem to be desirable that there be biogeographic distributions and ecological profiles of relatives of crop plants, with an initial focus on crops such as sorghum, sunflowers, and clover, with wild native relatives in the United States, where transfers of genes from engineered crops to wild relatives could occur.

It would also seem desirable that there be research on the overall ecology of crops, how their pollen moves, and how they transfer genes, to provide a base that will allow us to facilitate in a safe and realistic manner the movement to field testing and the movement to use of genetically engineered plants.

Let me finally address what I think is the most important of these three needs that agricultural biotechnology has. What I want to address is the need for more biological knowledge—molecular, cellular, organismal, and ecological, but especially molecular and ecological—for agricultural biotechnology. It is extremely inadequate. It is extremely thin as far as plant science and ecological knowledge exists at this stage. Biotechnology requires a molecular knowledge of biological systems to make the constructions that one does in this area, and for many of the agricultural applications we also need to have a knowledge of the ecological aspects.

Health care biotechnology has very successfully fed on the strong base of molecular and physiological biology knowledge of the mammalian and human system, generated by strong support by NIH—we heard that in the previous panel—and foundations focused on health, such as, for example, the Hughes Foundation with a base of approximately $5 billion. No such equivalent foundation exists in the agricultural area.

There has been minimal funding of agricultural research ever since about the 1950's, and that's part of the problem of the minimal base that we now have in the agricultural sciences.

I might mention as we go by here that we are focusing on the human genome, and I think that's an appropriate area for us to pursue, but we should not forget that there are genomes in the agricultural area: key genomes in animals, key genomes in plants, possibly genomes in insects, where some parallel activity in mapping and then sequencing could in fact synergize the activities that are going on in the human area. There are examples in the past where in fact agricultural science has led to significant inputs into the human area. I might mention as examples that streptomycin, as an antibiotic, was discovered as a result of agricultural research; I might mention that the first AIDS vaccine that was approved for clinical trials in fact came out of using an agricultural entity, an insect virus, in fact, as the production system, and there are other examples that I could provide.

I think it's important then, as we think about mapping and sequencing, that we don't forget that there are opportunities and needs in key plants, in key animals, and possibly key insects, that should be integrated with the human genome sequencing.

Let me give some examples of the inadequacy of Federal support for agriculture as opposed to biomedicine. USDA provides about $46 million a year for competitive grants for agriculture. These are distributed in amounts of about $46,000 per investigator. On the other hand, NIH has been approaching $5 billion a year for biomedicine, and distributes about $164,000 per investigator. The complexity of doing molecular biology in an agricultural or a plant system is no different from the complexity of doing it in a human system; in fact, the agricultural and plant situation is even more diverse when you think of maybe 50 different crop plants, 50 different animals, and a diversity of insects and diseases and weeds to be focused on.

Then we have been inadequately funding this area, and without an adequate base of science these tools that we've developed are not going to be able to be used to produce the promising things that one should hope to expect in the agricultural arena.

What I'd recommend is a plan to generate needed knowledge in the agriculture area. I think we need to substantially increase competitive grants which are now, as I said, about $50 million a year, and I'd suggest that over a 5-year period these be increased by steps to $500 million. This would only be 2 percent of the amount that was provided in recent years for subsidization of our agricultural crops.

These competitive grants should be open to all performers based on the quality and based on the relevance of their proposals—State institutions, private universities, Government laboratories, private institutes, and industry. The purpose of these grants would be for training, possibly 20 percent; for individual investigators, possibly 40 percent—it's individual investigators that make the exciting new discoveries and open up new areas, but it's also important to bring together a diverse group of disciplines to pursue those new areas, so I think we need Centers of Excellence in the agricultural area, and possibly 40 percent of these funds might go into Centers of Excellence.

How to administer such a competitive grant program is a difficult question. One would suggest that the Agricultural Research Service and the Cooperative States Research Service within the USDA probably is not the right home for administration. The NSF is possibly a place for these to be administered, but possibly even more appropriate would be a cooperative relationship across the National Science Foundation, the USDA, and possibly DOE. There has been some initial cooperation there, with about $5 million being made available for plant science centers jointly funded within the last year, or proposed to be funded within the last year, by the National Science Foundation, the Department of Energy, and USDA.

It is interesting that the request for these proposals brought forth 60 proposals with more than 1,000 key scientists in the plant sciences participating, so clearly there is an opportunity for Centers of Excellence activity in this area.

The other thing I think one needs to focus on is what the priority areas are for these Centers of Excellence. I would suggest that maybe these priority areas are new nonfood feed uses—we heard about that area from Dr. Merrifield this morning. It's an area that can give us an opportunity to balance our excess ability to produce agricultural crops with new markets outside the food and feed area.

The second opportunity, I think, is the biological control area and managed ecosystems. How can we develop biological controls to reduce our dependence on synthetic pesticides and the possible health and environmental and economic risks associated with those?

A third area might be higher value in used foods and feeds.

A fourth area might be increased productivity.

A fifth area might branch beyond agriculture and reach to some of the global change area, where one might look at carbon dioxide and greenhouse effects in terms of the agricultural component, in terms of minimizing those.

In summary, then, I've tried to leave with you three areas that I think are important for Government to help make our agricultural system more competitive in biotechnology. The most important one in my judgment is enhanced funding, with competitive grants for the agricultural areas so that we can deepen our molecular and our ecological base. The second area that I think is important is a favorable investment scene for the commercialization activity which we're now getting in place in the agricultural area. The third area is realistic regulation, where I think we've been making some progress to date.

Thank you.

[The prepared statement of Dr. Hardy follows:]

STATEMENT FOR U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE AND TECHNOLOGY
SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT
AND
SUBCOMMITTEE ON SCIENCE, RESEARCH AND TECHNOLOGY

July 14, 1988

Ralph W.F. Hardy
President
Boyce Thompson Institute
for Plant Research at Cornell
Ithaca, NY 14853

and

Deputy Chairman
BioTechnica International, Inc.
85 Bolton Street
Cambridge, MA 02140

It is a pleasure to participate in this hearing on biotechnology science coordination and competitiveness in HR 4502 and S 1966. My comments are based on my experiences as:

(1) President of a not-for-profit, private research institute, Boyce Thompson Institute for Plant Research at Cornell with a preeminent 64-year record in generating knowledge in the plant sciences and impacting agriculture with that knowledge. The first selective herbicide--2,4-D--was synthesized at the institute as part of a basic study of plant hormones and roots. This herbicide has been used for over forty years for weed control with cumulative sales of over $10MMM. The institute now combines molecular, cellular, organismal, and ecosystem biological studies of selected aspects of plants and their relationship to food and the environment. The research and resources of the Institute represent a microcosm of tomorrow's agricultural research, one in which fundamental scientific research and technological developments such as biotechnology and policy issues go hand in hand;

(2) President and now Deputy Chairman of a development-stage biotechnology company, BioTechnica International Inc., located in Boston with affiliates or subsidiaries in the Midwest, Canada, and the UK and focusses on genetically-engineered seeds and seed treatments for more productive crop agriculture and diagnostics for infectious diseases including periodontal disease where current treatment cost is $4MMM;

(3) Director of Life Sciences at DuPont from 1979-84 leading DuPont's research diversification into life science-based business.

My comments will focus on agricultural and forestry biotechnology and competitiveness. I support, in general, HR 4502 and S 1966 but prefer that a section on agriculture similar to S 1966 be added to HR 4502 to recognize the uniqueness and importance of agricultural biotechnology to the United States.

I will indicate my expectations for the impact of agricultural and forestry biotechnology and identify those areas critical for the future health of U.S. agricultural biotechnology. These are a need for expanded quantity and quality of molecular and ecosystems biology research to provide the necessary knowledge base for development of genetically-engineered agricultural products and for the efficacious and safe use of these products in managed ecosystems (farms, forests, etc.). The second need for ag biotechnology is the availability of a favorable investment environment to provide the necessary capital for the costly research and development of ag products and their regulatory approval. The third need is for a realistic regulatory process and the provision of information to assist in risk evaluation.

Impacts of Ag Biotechnology

I am strongly optimistic on ag biotechnology for several reasons. Ag biotechnology will increase productivity of commodity crops through decreasing costs of inputs and increasing yield so as to assure that favorable crop areas such as in the U.S. will be the low-cost producer.

Ag biotechnology will increase the value-in-use of feed and food by increasing the protein content of forages such as alfalfa, increasing the healthfulness of foods such as low-fat meats and increasing consumer preference aspects of foods such as flavor, color, and shelf life.

Of great importance to U.S. crop agriculture is the potential of biotechnology to generate plant products for new non-food markets such as speciality and commodity chemicals, polymers, fibres and liquid fuels. This area could, in the long term, expand ag markets to match our current ability to produce excess crops. Success in this area would not only have great economic impact but would be environmentally neutral for partial stabilization of atmospheric CO_2 concentration and slowing global warming. Ag biotechnology is expected to be environmentally neutral or benign in other areas including the biodegradability of biopesticides, and biopolymers and the reduction of nutrient contamination through the use of self N-fertilizing crops in place of fertilizer nitrogen.

In addition, it is important to recall that agricultural research has major impact directly on agriculture but also indirectly on other important areas including human health care. Antibiotics such as streptomycin were a product of basic agricultural research. Currently ag research on insect viruses has produced the first AIDS vaccine to receive approval for clinical trials. The biodiversity of the organisms studied by agricultural researchers suggests that the indirect impacts may be even greater in the future than in the past. For example, current genetic studies in the Boyce Thompson Institute of the pea plant have produced mutants that take up and store large quantities of iron. Understanding these mutants may provide critical knowledge on how humans handle iron, and thereby lead to providing health benefits for humans.

Needs for Agricultural Biotechnology

There is a major need for more biological knowledge at the molecular, cellular, organismal, and ecosystem levels--especially at the molecular and ecosystem levels--for agricultural biotechnology. The recent OTA report recognizes this need. The current knowledge base is inadequate and is of little depth at the molecular and ecosystem levels.

Biotechnology requires a molecular knowledge of biological systems, and many applications--especially those in agriculture--require an ecosystem knowledge since crop agriculture is a managed ecosystem. Health-care biotechnology has successfully "fed on" the strong base of molecular and physiological biology knowledge of mammalian and human systems generated by the strong funding support by NIH over several decades and by many foundations focussed on human health such as the Howard Hughes Foundation. Health-care biotechnology companies request that the current level of funding continue for biomedical research while ag biotechnology companies seek a major increase. Agricultural science, including plant science, has received less that minimal research funding since the 1950s except for a few areas. The human genome mapping and sequencing proposal should be supported but may continue this imbalance between human and other biology if a parallel effort is not included on key selected animal, plant, and insect genomes. The comparative information from human and non-human genomes may be very useful for human health care, agriculture, and other areas.

The complexity of genomes important to agriculture is orders of magnitude greater than that of the human. One need only recognize that there are probably at least fifty crop plants and fifty animals important to agriculture; and in addition there are many disease, insect, and weed organisms.

Yet, competitive grants to support agricultural research are smaller in dollar size of award and size of program and somewhat shorter in duration of awards. In FY 1986 the average award by the USDA competitive grants program for agricultural science was $46,000, by NSF for biological science was $70,000, by DOE for plant science was $72,000, and by NIH for biomedical science was $164,000 or 3.6 times that for agricultural science while the cost to do molecular science is not significantly different for agricultural and biomedical science. The total USDA competitive program for agriculture in FY 1946 was $49 million while that of NIH was $4,900 million, or 100 times that of USDA.

It is essential that a federal competitive grants program of adequate size be established so that our agricultural biotechnology industry (see below) will have the needed genes to develop commercial products. In testimony on December 15, 1987 to the U.S. House of Representatives Committee on Agriculture, Subcommittee on Department Operations, Research and Foreign Agriculture--I recommended competitive grants program for agricultural research be increased in a step-wise manner over the next five years from the current level of $50 million per year to $500 million per year. This amount of $500 million would only be 2 percent of the subsidization of crops in recent years and have the potential to provide products that may eliminate the need in the long term for subsidization. Furthermore, a competitive grants funding of $500 million for ag science is only one-tenth of that for biomedical science and only slightly larger than that projected for human genome sequencing. Such a competitive grants program should be open to all performers--state and private universities, government laboratories, and private institutes and industry--based on quality and relevance of proposals and investigators. Such competitive grants would be used for training (20 percent), for individual investigator research (40 percent), and for interdisciplinary centers of excellence research (40 percent). Administration should be outside, ongoing research initiatives of the USDA in ARS and CSRS so that this new initiative competitive grants program will not be in direct competition with ongoing initiatives. The recent modest plant science centers initiative involving cooperative activities of NSF, DOE, and USDA may be a model for administration.

It would be necessary to prioritize areas for the competitive grants program especially for interdisciplinary centers of excellence. Such priority areas might include new non-food/feed uses of crops, biological control in managed ecosystems, higher value-in-use food and feed, increased agricultural productivity and agriculture in the environment including global change.

The second need of agricultural biotechnology is a favorable investment environment to provide the capital for ag biotechnology companies especially the development-stage biotechnology companies. The commercialization structure is being put in place for ag biotechnology. There is a healthy mix of large established and development-stage companies with a critical mass of science-technology-development-commercialization experience focussed on agriculture with more product-market diversity than that of health care companies. Leading agricultural biotechnology companies are beginning to emerge. One expects that development-stage companies will be major leaders in ag biotechnology as they are in health care biotechnology.

Let me give you one example of commercialization plans that are being defined and implemented. BioTechnica Agriculture, a subsidiary of BioTechnica International, is focussed on seed and seed treatment products for increased productivity, decreased cost of production (or increased yield), and higher value-in-use feeds for four major crops--alfalfa, corn, soybean, and wheat--with direct marketing to farmers in the ten-state corn belt area.

The costs for BioTechnica and other ag biotechnology companies for research and development and regulatory approval will be greater per genetically-engineered new seed or seed treatment than for traditional seeds or seed treatments. For example, a genetically-engineered corn with high value-in-use or a seed may cost $10 million prior to marketing while a traditional new corn hybrid costs $2 million. The value-in-use for the genetically-engineered corn is expected to be substantially greater than the traditional hybrid and thereby enabler a higher seed price. However, the need for risk investment to meet the higher costs prior to marketing makes a favorable investment environment critical. The pre 1986 tax laws met, in part, this need for health care biotechnology companies through R & D limited partnerships. Agricultural development-stage biotechnology companies, one of the major U.S. resources in ag biotechnology, need such an environment if they are to deliver products as the health-care companies are doing. Furthermore, the lack of such adequate capital may encourage or cause the technology to move more rapidly outside the U.S.

The third need of ag biotechnology is in the regulatory area. Field research is progressing. From 1986 to 1988 plants with herbicide resistance, insect resistance, and disease resistance have been introduced into field research plots while genetically-engineered microbes with potential for physical stress and insect resistance and increased yield through enhanced nitrogen fixation have also been introduced.

An October 1987 workshop at Boyce Thompson Institute brought together molecular, cellular, organismal, and ecosystem biologists and lawyers from industry, government, universities, and public-interest groups to consider the regulatory requirements for field introduction of genetically-engineered crops. Risks to the environment and agriculture were considered while those for food and feed uses will be considered in a workshop planned for early 1989. The 1987 workshop focussed on major U.S. crops, near-term genetic-engineering changes, and introduction into the U.S. The conclusion was that there is negligible risk for most of the above major crops introduced into the U.S. for field testing and commercial use. Two major recommendations were made to provide a database to assist in field introduction decisions. It was specifically recommended that biogeographic distributions and ecological profiles be completed for the relatives of crop plants with an initial focus on crops such as sorghum, sunflower, and clover with wild relatives in the U.S. where transfer of genes from engineered crops to wild relatives could occur. In addition, research is needed to provide information on the overall ecology of crops including how their pollen moves and how their genes are moved. The report of this workshop, Regulatory Considerations: Genetically Engineered Plants, is available from Boyce Thompson Institute for Plant Research at Cornell, Tower Road, Ithaca, NY 14853. Senator Leahy's Senate comments on S 1966, as recorded in the Congressional Record of June 17, 1988, reference this report. It is important that an adequate database be available to enable a facilitated regulatory process for genetically-engineered plants so that real risks are avoided and unreal risks do not produce delays in regulatory approval.

In summary, agricultural biotechnology will provide needed new products and options for U.S. agribusiness and production agriculture. These products will be, in general, favorable to the environment in contrast to existing agricultural inputs. In addition, major indirect benefits are expected for non-agricultural areas--such as human health --as have occurred in the past. The U.S. is currently a leader in agricultural biotechnology but our base of strength is weak and has three significant needs that may be supported by S 1966 and HR 4502. The primary need is to develop an adequate base of agricultural science, especially at the molecular and ecosystem levels. A step-wise, expanded federal competitive grants program is recommended to meet this critical need. The second need is for a favorable investment environment to provide adequate capital for the R & D and regulatory approval of ag biotechnology products, especially by the agricultural, development-stage biotechnology companies who have inadequate to minimal capital. These companies, with their commercialization efforts being put in place, are expected to introduce many, if not most, of the ag biotechnology products as did their counterparts in health-care biotechnology. The third need if for a realistic regulatory process and an expanded database for decision making.

Mr. **Scheuer**. Thank you very much, Dr. Hardy.

Ms. Hollander?

STATEMENT OF ANNE HOLLANDER, CONSERVATION FOUNDATION

Ms. **Hollander**. Good afternoon. Thanks for the opportunity to comment.

I'm going to talk mostly about the proposal to form a National Biotechnology Policy Commission. I think the most compelling reason to support the formation of the commission that is described in H.R. 4502 and S. 1966 is really that it could serve as an important way to identify important potential benefits of biotechnology and to ensure that we develop them for the good of society.

Mr. **Scheuer**. May I interrupt you for just one moment?

Dr. Hardy, you didn't address the question of the commission in your very broad-ranging testimony. Do you have a position in support of it, in opposition, or whatnot?

Dr. **Hardy**. Yes. I think S. 1966 included in it a portion that addressed the agricultural area, and that I do not see in the House bill. I would like to see recognition of the agricultural aspect added to the House bill.

Mr. **Scheuer**. Very good. Thank you.

Please proceed, Ms. Hollander.

Ms. **Hollander**. Thank you.

I believe some beneficial products and uses of biotechnology might not be achieved in the absence of this or some other public sector initiative. Examples of this include a range of environmentally-safe alternatives to current chemical products and processes; products that will assist developing countries, such as stress-tolerant plants and vaccines for endemic diseases; and developments that will supply the world with effective, renewable energy sources.

Also, I would like to stress that the basic research component is something I would see this commission as able to facilitate, and I would strongly agree with Dr. Hardy's comments about the need for more basic research in ecology and in agricultural sciences.

My conclusion is that the proposed commission could play a role in ensuring that these benefits of biotechnology are realized in spite of what I see as current obstacles to their realization. What I will do in the next few minutes is just comment on what some of these obstacles are as I see them, and then at the end list some differences I see between the two forms of this commission as proposed in the two bills and make some comments about that.

There are a lot of potential benefits of biotechnology. They have been mentioned already this morning, and I think what I will do is skip over that part of my testimony. It's in the record, and as I said, it's been mentioned by a lot of other people.

I want to stress that by realizing those benefits, societies which are able to capture those benefits will realize a lot of benefits besides the direct ones. Second order benefits include things like increased export earnings, expanded employment opportunities, a healthier environment, and geopolitical advantages due to increased national income.

Mr. **Scheuer**. I suppose healthier people might be an advantage?

Ms. **Hollander**. Yes, obviously.

Now, the problem with all of this is that experience teaches us that scientific knowledge and technical ability to advance public welfare are not sufficient by themselves to assure the most desirable outcomes. Ultimately, economic and social forces rather than technical ones are the determining factors in whether society can or will constructively exploit a new technology.

For example, the fact that we have the capability to create safer industrial processes or the capability to produce products that can serve the needs of poor communities is not enough to ensure their development. Indeed, the inherent orientation of the marketplace, which is to turn a profit, tends to force the private sector to discard many potentially fruitful areas of research.

Given this historic experience, it's not surprising that some of the significant potential benefits of biotechnology may not be realized without public sector intervention. What I want to do is briefly describe five examples of this; I am sure there are many others that could be identified.

I think we are currently lagging when one considers the relative benefits in five areas, at least.

One, research on pesticides, narrowly targeted to single crops and pests.

Second, development of microorganisms for hazardous waste degradation.

Third, the creation of vaccines to control endemic diseases in developing countries.

Fourth, efforts to increase genetic diversity in major species of crops.

Fifth, development of more efficient renewable energy resources.

Each of these potential benefits is suffering right now from some obstacles, and as I mentioned, they vary. They include economic and social and political obstacles in each case. Let's take the first, the development of pesticides targeted to only one pest and one crop at a time, or to just a few.

Such pesticides are particularly beneficial because they are effective, yet they cause limited adverse effects; that is, they do not kill insect predators or cause human illness. The private sector has insufficient economic incentive to develop these kinds of pesticides, except perhaps for the four or five major food crops in the world and their primary pests. There are two reasons for this. First, the potential market for a narrow-spectrum pesticide is usually quite small compared to that for a broad-spectrum pesticide. Secondly, the fact that the public derives these health benefits from a safer product has little or no economic relevance in the marketplace. The marketplace tends to impose very similar financial and time costs for research, development, regulatory approval, and marketing on every pesticide product regardless of differences in environmental superiority.

The second important use of biotechnology would be to develop waste-degrading organisms. In fact, the first genetically engineered organism that was patented falls in this category; it went to the Supreme Court in the historic case of *Diamond* v. *Chakrabarty*. However, research on microbial products for waste degradation has received relatively little public or private funding. Technical difficulties seem to be part of the problem here, but an additional impediment is the tendency of the Superfund regulatory program to prefer existing methods, which include burning and burying wastes. This is partly because of the high public anxiety that attends hazardous waste problems, and it's also because the Government has a strong incentive to avoid any new waste disposal method, even very promising ones, because of the way the regulations work.

The third important breakthrough achievable using biotechnology is the development of human vaccines for a wide array of endemic diseases in developing countries. Beside the compelling moral reasons to do this, obviously the economic health of those countries has a strong bearing on our own economic health. We have lots of bank loans tied up in developing countries. But again, the inability of the end users in developing countries to pay for things that might benefit them has a strong dampening effect on the development of products like this.

In this case, liability concerns also seem to have a dampening effect. For example, when the President of Genentech was approached by the World Health Organization some years ago to participate in developing a vaccine for malaria, he declined—apparently because the potential economic gains were insufficient to justify the cost and the financial risk.

The fourth example of a public need which economic and social forces seem to disfavor is the need to increase genetic diversity in major species of crops. Breeding of genetically identical crops is actually increasing and will increase with the use of gene cloning, although it need not from a technical standpoint. This increases the vulnerability of crops to pests and diseases, and there are very good historic examples of this problem. The 1970 corn blight is the most frequently cited; in that case, the United States lost about a billion dollars, and more than half the corn crop. It seriously threatened the 1971 corn seed supply. In a similar vein, if some of the corn seed planted now in the United States were drought-resistant, the economic disaster we anticipate from the current drought might conceivably be reduced.

A final example of a public benefit that we should be supporting from biotechnology, and which may not be developed in a timely manner, is the need for new and more efficient energy resources. Public sector funds for research into energy alternatives have dwindled in the last decade, but in the long term the need for renewable and efficient sources of energy will certainly reemerge, although probably not in time to undertake the appropriate research and development. In other words, by the time public concerns are heightened again, we may be behind the important early curve that we need to get behind on this.

Again, it's really economics. The needs of future generations just don't factor into decisions that are made today in the marketplace, but it's clearly in our society's long-term interests to begin worrying about these problems sooner rather than later.

Again, those are just examples of benefits that we can achieve with biotechnology and some of the reasons we may not unless we have public sector intervention. I don't believe that those obstacles should be allowed to defeat or significantly delay the achievement of those benefits. For these reasons I am encouraged to think that the National Biotechnology Commission—that one of its most important functions could be to identify how these areas could be better addressed.

In that regard I want to note several differences between the House and Senate versions of this bill.

In the House version, H.R. 4502, a number of findings are listed that are apparently considered pertinent to the formation of the proposed commission, and those findings include statements such as the following, that "biotechnology may provide new methods for cleaning up hazardous wastes," which is one of the things I mentioned; it "may have significant benefits in meeting the needs of developing nations;" it "may reduce dependence on synthetic chemical pesticides," etc.; and "biotechnology processes and products must be developed in ways that are consistent with the protection of the environment."

I believe this or very similar language should be maintained in the final version of this bill, if at all possible. I noted that it was not presently included in the Senate version of the bill.

Lacking an explicit mandate to consider these issues, I think that one of the most important roles of the commission would be overlooked.

A second important difference between the two bills is that the Senate bill limits representatives on the commission to those from Government, industry, and universities. I believe the commission should include representatives of public interest groups as well. They have been instrumental in defining areas of public concern in the past, and if a major role for the commission is to define such areas in the future, their absence would constitute an important gap.

I also feel the commission will lack public credibility if it doesn't have public interest representatives.

Finally, I believe both bills would be strengthened if they included explicitly the statement that a variety of disciplines would be included on the commission, representing both social and biological sciences. I think the commission will be most effective in carrying out its responsibilities if it includes experts in economics and sociology, ethics, and policy, along with biologists and geneticists.

I think I will conclude my comments at that point, and I will be glad to answer any questions.

Thank you, Mr. Chairman.

[The prepared statement of Ms. Hollander follows:]

TESTIMONY OF ANNE K. HOLLANDER
ASSOCIATE, THE CONSERVATION FOUNDATION

BEFORE
THE SUBCOMMITTEE ON
NATURAL RESOURCES, AGRICULTURAL RESEARCH, AND ENVIRONMENT
AND THE SUBCOMMITTEE ON
SCIENCE, RESEARCH, AND TECHNOLOGY
OF THE COMMITTEE ON
SCIENCE, SPACE, AND TECHNOLOGY

REGARDING THE FORMATION OF
A NATIONAL BIOTECHNOLOGY POLICY COMMISSION

JULY 14, 1988

Good morning, and thank you for the opportunity to comment on the proposal to form a National Biotechnology Policy Commission as described in two bills currently pending in Congress (H.R. 4502 and S. 1966).

In my view, the most compelling reason to support the formation of such a Commission is that it can serve an important national need; namely, identifying the most important potential benefits of biotechnology and helping to ensure we will develop them for the good of our society. I believe some beneficial products and uses of biotechnology might not be achieved in the absence of such a public sector initiative. These include a range of environmentally safer alternatives to current chemical products and processes; products that will assist developing countries, such as vaccines for endemic diseases; and developments that will supply the world with effective, renewable energy sources.

In the first part of my testimony I will describe some of the important potential benefits of biotechnology. Then I will identify some economic and social forces that may delay or even preclude us from realizing those benefits. I conclude that the proposed Commission could play a role in ensuring that many benefits of biotechnology are realized in spite of these obstacles. At the conclusion I offer some remarks about a few differences between the two forms of the proposed Commission that are currently put forth in H.R. 4502 and S. 1966.

POTENTIAL BENEFITS OF BIOTECHNOLOGY

By some estimates, approximately 50% of agricultural yield increases achieved since the turn of the century are due to improved genetic characteristics. This is an indication of the potential of biotechnology, which opens entirely new avenues for improving genetic traits. Among the projected benefits and goals of research in crop breeding alone are better understanding of genetic and physiologic processes in plants, faster diagnosis of plant diseases, improved resistance to stresses (salinity, pests, diseases, drought, and flooding), and the ability to propagate species that are difficult to propagate vegetatively. Biotechnology can also be used to improve food quality through increases in nutritional content, and to increase food supply stability by introducing more genetic variability in plant varieties. Faster screening for desirable traits and faster breeding cycles can reduce the time from research and development to actual use.

Beyond the uses of biotechnology for improving crops, other projected benefits include new techniques to degrade the toxic chemicals in hazardous waste sites, methods to reduce or eliminate the wastes in streams leaving industrial plants, creation of safer alternatives to synthetic chemicals, development of alternatives to scarce energy resources, new approaches to conservation of genetic resources, and new pharmaceuticals to treat human and animal diseases.

Societies that capture these and other benefits will realize second-order benefits as well. These include increased export earnings, expanded employment opportunities, a healthier environment, and geopolitical advantages due to increased national income.

POTENTIAL OBSTACLES TO ACHIEVING BENEFITS

The benefits I have just described and many others I do not have time to mention are exciting to contemplate. However, experience teaches us that scientific knowledge and technical ability to advance public welfare are not sufficient to ensure the most desirable outcomes. Ultimately, economic and social forces rather than technical ones are the determining factors in whether a society can or will constructively exploit its technical knowledge. For example, the fact that we have the capability to create safer industrial processes, and/or the capability to produce products that can serve the needs of poor communities is not enough to ensure their development. Indeed, the inherent orientation of the marketplace -- which is to turn a profit -- tends to force the private sector to dicard many potentially fruitful areas of research.

Given this historical experience, it is not surprising that some of the significant potential benefits of biotechnology may not be realized unless the public sector intervenes to ensure otherwise. I will describe very briefly five such potentially important developments from biotechnology to illustrate my point. In each case, a different combination of economic, social, and political obstacles may cause either a long delay or an outright failure to realize an advance that would otherwise benefit society as a whole.

We are currently lagging (when one considers the relative benefits to be gained) in the following areas:

1. Research on pesticides narrowly targeted to single pests and crops,
2. Development of microorganisms for hazardous waste degradation,
3. Creation of vaccines to control endemic diseases in developing countries,
4. Efforts to increase genetic diversity in major species of crops, and
5. Development of more efficient, renewable energy resources.

A frequently cited advantage of genetic engineering is that it permits the development of pesticides targeted to only one pest and one crop at a time. Such pesticides are particularly beneficial because they are effective yet cause limited adverse effects; that is, they do not kill insect predators or cause human illness. However, the private sector has insufficient economic incentive to develop this use of biotechnology, except perhaps for the four or five major food crops and their primary pests. For the hundreds of other minor crops and pests, targeted pesticides tend to be poor business investments for at least two reasons. First, the potential market for a narrow-spectrum pesticide is usually quite small compared to the market for a multi-pest, multi-crop pesticide. Second, the fact that the public derives health benefits from the narrow-spectrum pesticide because of its safer environmental characteristics has little or no economic relevance to producers. The marketplace tends to impose the same financial and time costs for research, development, regulatory approval, and marketing on every pesticide product, regardless of differences in environmental superiority.[1]

---

[1] National Academy of Sciences, 1975, Pest Control: An Assessment of Present and Alternative Technologies, Vol. 1, "Contemporary Pest Control Practices and Prospects, The Report of the Executive Committee," National Academy Press, Washington, D.C., pp. 161-162; U.S. Environmental Protection Agency, 1976, "Incentives for Research and Development in Pest Control," National Technical Information Service, Springfield, Va., pp. 32-33.

A second important use of biotechnology is to develop waste-degrading organisms. Such organisms can be used to reduce human and environmental risks from toxic waste sites and to decrease or eliminate toxic by-products from industrial waste streams. The first genetically engineered organism to receive a patent (in the historic Supreme Court decision of Diamond v. Chakrabarty) was a microbe designed for exactly this purpose. However, research on microbial products for waste degradation has received little public or private funding. Technical difficulties are partly responsible, but an additional impediment cited by the waste treatment industry is the tendency of the Superfund program to prefer existing methods (burning or burying) over new methods of hazardous waste treatment. Because of the high public anxiety that attends hazardous waste issues, the government has a strong incentive to avoid new waste disposal methods -- even very promising ones.

A third important breakthrough achievable using biotechnology is the development of human vaccines for a wide array of diseases, especially those that afflict a large proportion of the world's population living in tropical countries. The opportunity is compelling to reduce human illness from diseases such as schistosomiasis, onchocerciacis, malaria, and others, and international organizations like the World Health Organization are making some progress in developing such vaccines. Again however, the inability of end-users to pay for these products has a strong dampening effect on their development, and liability concerns create an added disincentive to enter this field of product development. For example, when the president of Genentech was approached by the World Health Organization to participate in developing a vaccine for malaria, he declined -- apparently, the potential economic gains were insufficient to justify the cost and the financial risk.[2]

A fourth example of a public need which economic and social forces seem to disfavor is the need to increase genetic diversity in major species of crops. Breeding of genetically identical plants is encouraged by most plant breeding activities and is becoming even more prevalent with gene cloning. However, it increases the vulnerability of crops to disease and pests, with some historically serious consequences for management of stable food supplies. The 1970 corn blight in the United States is but one example. The blight cost farmers about $1 billion in losses and some Southern states lost more than half their crop; it also seriously threatened the 1971 corn seed supply.[3] In a similar vein, if some of the corn seed currently planted in the United States were drought resistant, the economic disaster we now anticipate from the drought of '88 might be reduced.

---

[2] John Elkington, 1986, "Double Dividends? U.S. Biotechnology and Third World Development," World Resources Institute, Washington, D.C., p. 10.

[3] Jack Doyle, 1985, Altered Harvest: Agriculture, Genetics, and the Fate of the World's Food Supply, Viking Penguin Inc., New York, pp. 1-15.

As a final example of a public benefit from biotechnology that may not be developed in a timely manner unless public assistance is provided, consider the need for new and more efficient energy resources. Public sector funds for research into energy alternatives have dwindled in the last decade as public concern has dropped (along with the price of oil). In the long term the need for renewable and efficient sources of energy will certainly reemerge -- although probably not in time to undertake the appropriate research and development. The needs of future generations do not generally factor in to the research and development decisions of corporations competing in today's economy, but it is probably in our society's long-term interest to begin worrying about those needs sooner rather than later.

CONCLUSIONS REGARDING THE MERIT OF A NATIONAL COMMISSION

I believe that social and economic obstacles such as those exemplified in the above examples should not be allowed to defeat or significantly delay the most publicly worthwhile uses of biotechnology. Instead, we should establish mechanisms to objectively identify these obstacles and craft and implement appropriate public sector interventions. For these reasons I am encouraged to know that Congress is considering establishing a National Biotechnology Policy Commission. I believe such a Commission could serve this role well. In particular, it could advise the President and the Congress about economic and social trends that are influencing the direction of biotechnology research, and make recommendations for redirections where appropriate.

DIFFERENCES BETWEEN H.R. 4502 AND S. 1966

I would like to conclude with a few words about the differences between H.R. 4502 and S. 1966, both of which currently contain language that would establish a National Biotechnology Policy Board or Commission. Several of the variations in wording seem quite important.

First is the fact that H.R. 4502 lists a number of "findings" pertinent to the formation of the proposed Commission. These findings include the following:

> "Biotechnology may provide new methods for cleaning up hazardous waste sites and aiding the management of natural resources,"
>
> "Biotechnology may have significant benefits in meeting needs of developing nations for food, fiber, and fuel,"
>
> "Biotechnology may reduce dependence on synthetic chemical pesticides and fertilizers which may pose threats to the environment...," and
>
> "Biotechnology processes and products must be developed in

ways that are consistent with the protection of the environment."

I believe that this or similar language should be maintained in the final version of this bill if at all possible (it is not presently included in S. 1966). Lacking an explicit mandate to consider how research may need to be guided into specific areas of public need, the Commission's role could be limited to coordination and advancement of research in general. The former role, in my view, is the most important one for such a Commission and I hope it will be explicitly stated.

A second important difference between the two bills is that H.R. 4502 requires that the Commission include representatives of public interest groups, whereas S.1966 is limited to representatives of the government, industry, and universities. I believe the Commission should include representatives of public interest groups. They have been instrumental in defining areas of public concern in the past, and if a major role for the Commission is to define such areas in the future, their absence would constitute an important gap. Further, I feel the Commission will lack public credibility if it does not include representatives from the public interest community.

Finally, I believe both bills would be strengthened if they required that Commission members represent a variety of disciplines in the social as well as biological sciences. In particular, I think the Commission would be most capable of carrying out its assigned responsibilities if it included experts in economics, sociology, ethics, and policy along with biologists and geneticists. All these disciplines have much to offer in analyzing long-term trends in biotechnology and making appropriate policy recommendations.

Thank you again for the opportunity to comment on the proposal to create a National Biotechnology Policy Commission. I hope my comments have been helpful and I would be pleased to answer any questions you may have.

The Conservation Foundation

ANNE K. HOLLANDER is an Associate at The Conservation Foundation, where she conducts interdisciplinary policy research on emerging issues in environmental and resource management. Her areas of expertise are biotechnology, science policy, pesticide use, and agriculture.

Ms. Hollander is recognized as a national expert on U.S. biotechnology regulatory policies. From 1983 through 1986, she served as the first Biotechnology Program Manager in the Office of Toxic Substances of the U.S. Environmental Protection Agency. In that position, she had a lead role in developing the policy and scientific aspects of EPA's programs governing the environmental release of genetically engineered organisms. She managed the preparation of EPA's statements of proposed and final policy on biotechnology, and worked with the Department of Agriculture and the Food and Drug Administration on numerous inter-agency issues that arose during the formulation of that policy.

From 1980-1982, Ms. Hollander served as an Environmental Policy Analyst, and later a Pesticide Review Manager, in EPA's Office of Pesticide Programs.

Ms. Hollander graduated from Stanford University in 1979, earning her B.A. and her M.A. in the same year. Her graduate degree was earned from Stanford's Food Research Institute, which is devoted to interdisciplinary study of agricultural development and resource issues. As an undergraduate, Ms. Hollander designed her major in International Public Policy by combining coursework in political science, economics, and ethics.

1250 Twenty-Fourth Street, NW Washington, DC 20037 USA 202/293-4800 Telex: 64505 PANDA
Affiliated with World Wildlife Fund

Mr. **Scheuer**. Thank you very much, Ms. Hollander.

Dr. Mackler?

STATEMENT OF DR. BRUCE F. MACKLER, ASSOCIATION OF BIOTECHNOLOGY COMPANIES

Dr. **Mackler**. Thank you very much, Chairman Scheuer.

Mr. **Scheuer**. As I said before, and this goes for both of the last two witnesses, don't hesitate in giving us a summary of your testimony to refer to anything you've heard here today, including the first two witnesses on this panel.

Dr. **Mackler**. I'd be delighted to.

Mr. **Scheuer**. Thank you.

Dr. **Mackler**. I would like to say that ABC is delighted to be here today. We believe these bills are extremely important because they will provide the framework for the advances to fuel the commercial development of biotechnology for the next 20 or 30 years, as well as the products that will be derived to help mankind.

Let me introduce myself. I am general counsel for the association. Let me introduce the association because ABC is a young association. We have grown in four and a half years from eight companies up to over 182 now, worldwide. We include very large companies which are multinational, as well as extremely small companies.

Mr. **Scheuer**. Tell us something about "worldwide" and "multinational." You represent biotechnology companies around the world?

Dr. **Mackler**. We have CIBA-GEIGY, with their U.S. subsidiary; we also have companies around the world who belong to ABC. About 20 percent of our membership is outside the United States.

Mr. **Scheuer**. Any of them in Japan?

Dr. **Mackler**. No, unfortunately, but we do have Japanese companies in the United States that belong.

Mr. **Scheuer**. Perhaps in the course of your testimony you can give us, from your point of view—from the point of view of the private corporation—some concept of sharing knowledge. When do you share? When do you hoard? What are the cutting-off points? How can we expedite the process by creating this whole that is greater than the sum of the parts, getting global expertise and global scientific talent and imagination involved in some way where we preserve a perfectly clear, unfettered role for the private sector to go ahead and do its thing with perfectly legitimate private sector financial incentives and rewards out there? It seems to me that the two of you can give us some real insight and wisdom on the question of what we share and what we hoard, how we doff our hats to the free enterprise system, the profit system, as a means of triggering all of this talent and all of these resources? And how do we define the point at which sharing stops and the free enterprise community takes over maximally to move the whole process forward?

Dr. **Mackler**. Yes, I'll try to touch on that.

That is very important to us. The average size of U.S. biotechnology companies is 100 employees, excluding the multinationals, of course. So uniquely, the biotechnology industry is a small-company industry in the United States, as well as in a few other parts of the world, excepting Asia and some parts of Europe. That's an interesting thing to remember in terms of the impact of this bill on the industry.

Secondly, ABC also now includes a Council of State Biotechnology Centers from around the United States. These are the centers doing the technology research, the technology transfer, as well as informational research.

The composition of ABC is important because we cover the whole gamut, from very large firms to very small firms, from service groups that are impacted to the commercial research groups that are impacted.

The association supports establishing development and responsible growth of biotechnology industries as a national priority. We recognize the need for this. We have repeatedly asked the Administration for a statement of national priority, as has been done in Europe and Japan; this has not been done. We feel that H.R. 4502, as well its companion bill, S. 1966, are excellent starting points to create a much-needed, Government-wide effort to meet this goal, and I'll touch on how we feel this should be done.

I'd like to take the remaining time just to touch on some points. Let me start on the National Center for Biotechnology Information.

We believe the National Center described in S. 1966 can provide critical information to academic and commercial biotechnology research communities, and should be included in your subcommittee bill.

I would like to make the following suggestions to add to the bill.

First of all, the mere collection of data—I'm a scientist before I became a lawyer. We all publish papers, and I always like to go back to the citation index to see who references my papers. The measure of intellect is what you really have contributed. It is devastating sometimes; you think your papers are very key, and they're not referenced. Other papers which you thought were not key are referenced. Therefore, just to produce a lot of data, to create a large collection mechanism, is not an end point. The end point has to be how to use the data. Here again is a very important problem. The computer system——

Mr. **Scheuer**. How to use the basic raw material of fundamental, basic research——

Dr. **Mackler**. No, how to use the data generated, all those sequences. Today we have talked with a number of our members, several of whom are doing genome sequencing, and they have told us that computer systems today do not allow good retrieval of the data. You cannot compare your systems very easily. So therefore, just emphasis on bringing the data in, is not sufficient; you must have emphasis for the long term on state-of-the-art computer systems and software systems that can allow you to utilize the data effectively in terms of comparing it and retrieving it in a usable format.

Mr. **Scheuer**. Are we doing that nationally?

Dr. **Mackler**. No, we're not.

Mr. **Scheuer**. The next question is, Are we doing that internationally?

Dr. **Mackler**. It is being done by several small companies who are working on PC software data base programs. But it is not, we feel, a concerted effort, and this should be part of the bill.

Next——

Mr. **Scheuer**. Excuse me. Let me just interrupt you to suggest informally to Dr. Kirschstein, when we get to the questions and answers maybe we will invite you to come back and address the question of how NIH is encouraging the development of data, both nationally and internationally, that is comparable, so that we can compare apples with apples and not apples with peaches.

Dr. **Mackler**. Well, if I may comment, the problem is, the data base question is very big. We have small companies who are working on software. It is so big that small companies in themselves cannot do it. They can do pieces of it. You do need a large program that is coordinated, but you need a program that involves the companies who are developing the software now to be integrated into that program.

One of the suggestions we are going to make is the integration of the industry into this whole program. We feel it is key, and especially since they are small companies, just like the Japanese have done, we can utilize this program to fuel the economy and to fuel these companies, and they can make contributions. They are very well-focused contributions because these are the experts. These are the people with the hands-on experience.

We differ very much from the administration's view that industry people should not be included. They should be included at all levels that are reasonable and don't compromise confidentiality.

Mr. **Scheuer**. Well, I just couldn't agree with you more, and we have just got to find the Government institutions and the Government systems and processes that not only permit that but then encourage that. It is absolutely aberrational for us to say no to industry/Government/nonprofit/environment groups, collaboration among the above. It is absolutely aberrational, and defies logic and defies experience.

Dr. **Mackler**. We totally agree, and one way we would like to suggest, to be included in the bill, is a mandated industry steering committee to work with the library staff on designing the outreach program to integrate the industry's participation. This would be to include things like recommending data format, recommending computer systems and how they should be usable by the companies, recommending how access can best be made by the industry for the information.

Mr. **Scheuer**. Is Dr. Kirschstein listening to this? This is the kind of thing we want you to respond to.

Dr. **Kirschstein**. Yes, sir. That's why I'm making notes.

Dr. **Mackler**. Secondly, we feel that this ISCE should include a cross-section, as your fellow from Berkeley testified, to involve all sections of the industry, and this should include small companies, large companies, the biotech centers and the academic researchers. They should be the people really involved in showing the library where the work should go, how it should be used. It is an academic-based industry but it is an industry, and therefore you must have strong industry comment and participation.

Secondly——

Mr. Scheuer. Do you mind having some involvement and comment by Ms. Hollander and her confreres in the nonprofit groups, the consumer, the health, the environment, the ecology groups?

Dr. Mackler. We believe it is an open dialogue, and that all parts of society have a vested interest in both the risks and the benefits of biotechnology and should participate, but the commercial applications, the actual utilization of the data is a commercial utilization. Therefore, the system should be geared toward the commercial issues, not the ethical issues. Those, we feel, are better placed in another mechanism which I will talk to you on in a minute.

Finally, we believe access should be on a reciprocal basis and open to all cooperating countries and groups. This should be emphasized. However, we would add a caveat that any group not giving access should not get reciprocal access, and we will be very candid about that. However, we don't think that is really a problem. As a scientist previously, we all rush to publish. If we have a sequence, we are going to get it published one way or another. The issue here in some cases——

Mr. Scheuer. You might even say, "publish or perish."

Dr. Mackler. So we don't believe that there will be international barriers to access, just because of the inherent academic nature of the accumulation of the data, but it is an issue that has to be thought about.

Let us now turn to the human genome and plant genome research. ABC supports the establishment of panels and funding of human genome research, but we have several major concerns. First, having been on the NIH study section, having been in the grant mechanism and for many years been an investigator myself, I am very concerned and I think the industry is very concerned: Where is the money going to come from? This is a very ambitious program.

Congresswoman Morella's question was very well taken. We are very concerned that as this program builds up, it will come from the individual grants known as the RO-1's. This we think would be devastating to the scientific community, whether it is to the individual scientist in academics or individual scientist in industry.

We also looked at the USDA budget, and we don't find there is very much fat in the USDA budget to support plant genome work, either. This concerns us, so the issue is to have a clear understanding, especially in these economic times: Where is the money going to come from for these projects? We can't rob Peter to pay Paul.

Secondly, ABC——

Mr. Scheuer. I think we just have to assume that we have to invest more funding in the scientific establishment.

Dr. Mackler. Yes.

Mr. Scheuer. The entire science institution in this country, the science community, has been underfunded. We have to stop that, and we have to get on with it fast. We are going to write our report with a view to making it available to the top program and policy people of both Presidential contenders. This is not a subject of partisan politics. This is a subject, in a real sense, of national survival, at least as far as our economy is concerned. We hope that we are going to have a very trenchant set of recommendations on the funding levels that should be involved here, as a matter of protecting the stability and the viability and the strength and the integrity of our economy, long-term.

Dr. **Mackler**. Thank you.

I may just add a comment there. You know, the biotechnology industry is really a child of the investments that the Government made, the U.S. Government in particular, made in the fifties and sixties for research, and one of the problems—speaking to your issue—if we don't continue to prime the pump, we will not have the research data base in the future for new advances in biotechnology in other areas.

Let me move on to the second area, the area of genome mapping and sequencing. There is sufficient technology today to do the mapping. The technology is there and a lot of companies are doing it.

We are concerned that a premature emphasis on sequencing would not be appropriate because of the lack of available technology. The development of sequencing technology and equipment should be done, we believe, through a Government-sponsored industry research and development program, in which those companies now very much involved in this area work with the Government groups and get funding to push their area of expansion and growth, to provide the technology and the equipment to be competitive.

We are very concerned because we find that some of the agencies do not see the biotechnology industry as a contractual partner, but rather as a passive observer to a Manhattan-like laboratory complex. We are talking about 500, 1,000 scientists doing sequencing somewhere. A Manhattan Project would not be appropriate, but the full involvement of the industry would.

To monitor the genome research, ABC supports the panels that have been suggested, but we also say the inclusion of university and industry representative should be paramount in these panels.

Let me move to the International Biotechnology Commission. We concur, the industry concurs with the congressional language directing national policymakers to make responsible growth and development of biotechnology a national priority. I may point out, as the OTA report pointed out, a lot of States are already making this a major economic policy in their economic growth.

It is important that Congress and the administration provide a strong mandate for development to this industry. Right now there is no mandate, and the absence of a mandate is very disconcerting because of the differences, the lack of leadership in the different agencies. I may point out that without a mandate——

Mr. **Scheuer**. Excuse me, Dr. Mackler. It is important for me to get this roll call vote. That is my mandate, so I am going to have to suspend for another 12 or 13 minutes, and I just ask you all to bear with me. It is a marvelous panel.

[Recess taken.]

Mr. **Scheuer**. Okay. We have had our last roll call vote, so we won't have any more interruptions from that point of view, and I want to thank you all for having hung in here as long as you have. It has been a marvelous panel.

Dr. Mackler, why don't you take as much time as you may need to finish up, and then we will hear from Mr. Godown, and then we will hear from the folks in the middle of the front row.

Dr. **Mackler**. Let me just pick up the thread.

We consider that without a national priority, confusion will continue to grow within the Government concerning the coordinated framework. ABC sees the consensus policy within the administration being eroded by the separate agendas of each regulatory agency. This is very disturbing.

There is no consensus, and if there is no consensus on the inside by the regulators, what is the industry supposed to do on the outside? You have to anticipate 5 or 6 years down the road. How can you predict what you are going to need, when even the Government doesn't know what they want? When they feel they are going down a path, it is one step forward, two steps back. That is very disturbing and it is very unsettling, especially for a small industry.

Going back, and I can't pronounce it, Dr. Yoshikawa's statement is concerning the need for industry to know and the need for industry to have long-term information. The whole lack of a consensus, of a direction in the agency, denies the industry the ability to make long-term commitments, even if they could or wanted to.

Mr. **Scheuer**. Well, you know we heard from Dr. Bruce Merrifield, who gave us excellent testimony, but I couldn't detect any sense on his part that we needed better interagency coordination or that we really needed the involvement of industry anyway in this consensus-building process on goals, on means, on priorities.

Dr. **Mackler**. Well, everybody has their own view. Obviously the administration views, which you have heard today, as well as the OMB view and the Department of Justice view on several issues, are not very consistent with what a lot of other people feel.

Mr. **Scheuer**. I wonder what Dr. Ruth Kirschstein thinks about this need for more interagency coordination, more involvement of the private sector in the process of setting priorities and setting goals and defining purposes? But we will hear from Dr. Kirschstein in just a few minutes, after we hear from Mr. Godown.

Dr. **Mackler**. Let me just hit my final points.

On the National Biotechnology Commission, on H.R. 4502, we believe that this is an excellent approach. We also believe that some other issues should be factored in.

First of all, we would love to see a sunset provision in it. Commissions go on infinitum, and by having a sunset provision there is a way of reassessing it periodically.

Mr. **Scheuer**. I totally agree.

Dr. **Mackler**. Secondly, it is important that the commission have definable links with international decision bodies—OECD, EEC. There should be some briefing or interactions between those, as well, because we are not operating in a vacuum.

Thirdly, and this is rather important, we believe an analysis of all existing governmental regulations and programs and new proposed regulations should be done in terms of how they impact on the national biotech priority. So if we are going to create a priority on one hand by a commission, now let's measure how the agencies are doing in reference to that priority, because a priority existing on its own has no relationship to the actualities many times, of what the agencies do.

Also, the commission should have a statutory component of large and small companies to reflect the full heterogeneity of the industry. As again Mr. Yoshikawa said, different companies have different agendas based on their economics, where they are in their development, and any sampling of the industry must take those differences into consideration.

Finally, on the reauthorization of the Biomedical Ethics Board, we believe—getting back to another issue you brought up and to public participation—we believe the Biomedical Ethics Board can provide a much-needed forum for public debate. However, as structured in the Chiles bill, one problem with this ethics commission is that it could stop, just by doing nothing, all the reports, all the recommendations made by panels. We believe that it should have a requirement to refer documents out within a set period of time, and we would say 45 days.

Secondly, we would recommend that all the documents get published in the Federal Register for public notice, so the public can see what is going on, and one of the problems right now that we are facing as an industry, is that we have a lot of emotionality injected. The emotionality is crippling the growth because there is not a proper forum for it, and apparently the forum that has been chosen is inappropriate—the courts. What we need is a proper forum, and I think the Biomedical Ethics Board could provide a forum so we could avoid lengthy court fights. We could have all the different components participating in the dialogue.

Let me close in terms of information sharing. We talk about information sharing in biotechnology. I want to tell you a story. I used to have post-docs when I ran a lab, and one of the nice things about post-docs is that they leave——

Mr. **Scheuer**. You are talking about postdoctoral——

Dr. **Mackler**. Postdoctoral fellows, yes.

Mr. **Scheuer**. Yes.

Dr. **Mackler**. One of the nice things is, they form a family, and it is an extension, your training of them is an extension of your own lab. One of the problems is, when they leave the lab they take half your lab with them. They take your cell lines, they take your chemicals, your reagents. This is not a negative. This is a positive, because they are going off to set up their own lab, to continue the work that you have trained them for, so there is built into the academic community a natural sharing of intellect through these types of mechanisms.

When you get down to the corporate level, the sharing of intellect is based on the value, the commercial value of the intellect. Now one shares through academic presentations the basic data. One also shares through the patent process the basic data, and it goes back to a point you made earlier today: If 7,000 patent applications are backed up, there is very little sharing of that data. The concept of the patent is to give you a monopoly so the public can then build upon that knowledge for new patents, new concepts.

So how do you share? First of all, you have to share. You have to have open access, but you have to have patents. The patent process has to be speeded up.

Secondly, we feel as an industry, for the security of the investment that the private industry is going to make, and also to facilitate the subsequent investment of the commercialization of the intellect which is being discussed here—to get it into products—there has to be some proprietary protection. So patenting of the genome sequences in relationship to their therapeutic, in relationship to their diagnostic value, should be allowed.

Let me close by just one further remark. I am very concerned by this administration's attitude not to include the private sector. One of the concepts is that this administration originally started out with the concept of including the private sector, of moving some of the responsibility from the Government to the private sector.

We believe that the inclusion of the private sector, especially in this type of industry, is very important. They are the experts. They understand the technology. The industry, the administration, is learning. Why should we learn separately? As you pointed out in your analogy with the chemical industry, if we learn separately then we may be antagonists rather than protagonists, so therefore I agree that industry should be involved at all appropriate levels in these committees and in any economic endeavors.

Thank you.

[The prepared statement of Dr. Mackler follows:]

Statement of

Bruce F. Mackler, Ph.D., J.D.

General Counsel

ASSOCIATION OF BIOTECHNOLOGY COMPANIES

Before The

Subcommittee on Natural Resources, Agriculture
Research and Environment

Committee on Science, Space, and Technology
UNITED STATES HOUSE OF REPRESENTATIVES

on

H.R.4502, the Biotechnology Science Coordination
and Competitiveness Act of 1988

and

S.1966, the Biotechnology Competitiveness Act
of 1987

July 14, 1988

The Association of Biotechnology Companies (ABC) is pleased to be given the opportunity by this Committee to comment on H.R. 4502 and S. 1966. ABC believes that these bills can provide a useful framework to promote the development and applications of new frontiers for biotechnology into the twenty-first century.

My name is Bruce F. Mackler and I serve as General Counsel to the Association. In addition to my law degree, I have a doctorate degree in Immunology and have published some 100 scientific articles and abstracts.

ABC was established five years ago by six biotechnology firms to promote continued innovation and responsible growth in the biotechnology industry. Today ABC represents biotechnology companies, biotechnology service and equipment companies, academic centers, and research institutes. ABC members utilize these technologies in a broad range of commercial applications-human health care, gene probe diagnostics, biotherapeutics, animal husbandry, agriculture, specialty chemicals, and other areas.

ABC has 180 members located in the U.S. and internationally. ABC's U.S. members are evenly distributed throughout the country, with one-third on the West Coast, one-third in the Midwest, and one-third on the East Coast.

ABC represents a diversity of biotechnology companies ranging from multi-national corporation to smaller companies. The average number of employees per U.S. biotech company, excluding multinationals, is about 100. Therefore, the U.S. biotechnology industry is a small-company based industry.

ABC also has a Council of State Biotechnology Centers which has eleven members. These centers serve as this country's incubator for startup companies new technology, research programs, and information collection.

The majority of ABC's members are biotechnology companies or biotechnology centers, specifically engaged in the use of human genetic material to develop diagnostics, biopharmaceuticals, and therapies. For that reason, the composition of the Association's membership makes ABC uniquely qualified to comment on the legislation pending before your Subcommittee. A list of our members is attached.

The Association of Biotechnology Companies supports establishing the development and responsible growth of the biotechnology industry as a national priority. Recognition by Congress and strong leadership by senior Administration officials of the promise of this new technology is imperative. ABC has urged senior Administration officials to make a strong public commitment to biotechnology as the Japanese and European governments have done. **Your legislation, H.R.4502, and Senator Chiles' bill, S.1966, are excellent starting points to create a much needed, concerted government-wide effort to meet this goal.**

I would like to spend the remainder of my time outlining for you comments on the bills before you. The Association and its members believe these bills can result in establishing biotechnology as a national priority.

NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION

ABC recently surveyed its membership to determine their immediate priorities. The majority of members ranked access to technical information and access to finance for research and development among their major issues. We believe that the National Center for Biotechnology Information described in S. 1966 can provide critical information to the academic and commercial biotechnology communities and should be included in your Subcommittee's reported bill.

To provide better access to the Center's information for the biotechnology industry, I would like to make the following suggestions for additions to H.R.4502/S.1966:

(1) The mere accumulation of genome data is not enough. There must be emphasis on new state-of-the-art computer programs to retrieve the data in useful formats.

Just as the Senate Report on S.1966 does, your Subcommittee bill (and accompanying report) should emphasize the importance of data retrieval.

This is currently a technical limitation which jeopardizes the ultimate utility of the project.

(2) ABC recommends the inclusion of an industry steering committee (ISC) to work with Library staff on designing an outreach program to alert industry about the Center, on recommending a data format and computer system usable by the biotechnology firms, and recommending how the information at the Center can best be accessed.

The ISC should be composed of a cross section of the biotechnology industry. Participants from small startup companies, larger corporations, Biotechnology Centers, and academic researchers.

(3) Reciprocal and open access to the Center's information to all cooperating countries should be emphasized. Biotechnology is an international science and both U.S. and foreign companies should have access to a comprehensive data base. However, countries which deny U.S. companies and researchers access to their genome database should not have reciprocal access. We believe that national barriers will not be a problem, since researchers will want to rapidly publish the sequence data irrespective of whether they would in the U.S., Europe, or Japan.

The Association would like to offer its services to the Library to help in coordinating the gathering of biotechnology information on such an international basis.

HUMAN AND PLANT GENOME RESEARCH

ABC supports the establishments of the Panels and funding of genome research, provided that several major concerns are addressed. I know that several of you share these concerns:

> First, where will the money to finance this ambitious program come from? ABC is concerned that funding for this project will come from the NIH budget which would decrease the NIH funds available for individual competitive research grants (RO-1s). USDA research appropriations do not have the "fat" to support the plant genome work either.
>
> Second, ABC supports the mapping of the genome which is within the current technology. A premature emphasis on the actual sequencing will face a lack of available technology. The development of sequencing technology and equipment should be done through a government supported industry research and development program. The emerging biotechnology industry should be a contractual partner in developing the technology, rather than a passive observer to a Manhattan project-like laboratory complex.

To monitor the genome research, the Association supports the creation of the human and plant genome panels. The inclusion of university and industry representatives on these panels is applauded. I would like to suggest that the first order of business be to focus on the how the mapping and sequencing of these genomes can be privatized.

You may believe that these issues are too technical for your attention at this time. I submit to you that they are quite appropriate and must be adequately addressed as you incorporate S. 1966 in H.R. 4502, to make the Subcommittee bill an effective vehicle that will stimulate growth of the biotechnology industry.

NATIONAL BIOTECHNOLOGY COMMISSION

The biotechnology industry concurs with Congressional language directing national policy makers to make responsible growth and development of biotechnology a national priority.

The State of California has already decided that biotechnology is a key industry worthy of top priority focus. ABC members have seen that the State's efforts to coordinate regulations and governmental policies in the California Framework proved helpful.

The Office of Technology Assessment's report release Tuesday identified 33 States which are actively engaged in encouraging the development of biotechnology. States have invested $147 million this year, but OTA does not see this thrust as sustainable without the federal government providing a clear message of support.

It is important that both Congress and the Administration provide a strong mandate for the development of this industry. Right now, no such mandate is evident to the industry.

Without a national priority, confusion will continue to grow within the government "coordinated framework." ABC sees the consensus policy within the Administration being eroded by the separate agendas of each regulatory agency. There must be unity of approach and purpose, not constant infighting and posturing.

The National Biotechnology Commission (H.R.4502) addresses this need. The Association's recommendations on the Commission include:

(1) The Commission creation should have a sunset provision.

(2) It is important that this Commission has definable links with key international decision bodies, such as the OECD and EEC. At least, an annual briefing by the Commission of such parties should be included.

This industry is international in scope. It should be a goal of this Commission to seek a harmonization of U.S. patents and regulations with the different countries.

(3) An analysis of all existing governmental programs and new regulatory proposals should be done in terms of how they impact on the national priority of biotechnology.

The criteria to measure governmental policies should be how well such policies reflect the Commission's recommendations.

(4) The Commission should have a statutory complement of large and small companies to reflect the full heterogeneity of the industry.

BIOMEDICAL ETHICS BOARD

ABC applauds the revitalization of this Board. Such a board would have been the best means to debate the issue of patenting life. Without this forum, there will be continued emotional public posturing and position taking, to the detriment of researchers, industry, and society.

Reauthorization of the Biomedical Ethics Board will provide a much needed forum for public debate; however, as structured in Chiles' bill, this Board could "stop" all reports and recommendations made by the two Panels and the Biotech Policy Board. The legislation could be improved by providing a specified time of review (45 days) once documents are referred to the Ethics Board. All reports and recommendations by this Board should be published in the Federal Register.

Members

INSTITUTIONAL MEMBERS

CURRENT AS OF JUNE 30, 1988

Agouron Pharmaceuticals, Inc.
La Jolla, California

Alfred Benzon, Inc.
Philadelphia, Pennsylvania

Allelix Biopharmaceuticals
Mississauga, Ontario
Canada

Alpha 1 Biomedicals, Inc.
Washington, D.C.

American Bio-Technologies Inc.
Cambridge, Massachusetts

American Cyanamid Company
Wayne, New Jersey

American Type Culture Collection
Rockville, Maryland

Amersham Corporation
Arlington Heights, Illinois

AMRAD Corporation Limited
Abbotsford Victoria
Australia

Antibody Associates
Bedford, Texas

Applied bioTechnology, Inc.
Cambridge, Massachusetts

Applied Microbiology, Inc.
Brooklyn, New York

Automedix Sciences, Inc.
Torrance, California

Becton Dickinson
Immunocytometry Systems
Mountain View, California

BioCarb AB
Lund, Sweden

Bioclone Australia Pty. Ltd.
Marrickville, NSW
Australia

BioEnterprises Pty. Ltd.
Roseville, NSW
Australia

Biometric Research Institute, Inc
Arlington, Virginia

Biomira, Inc.
Edmonton, Alberta
Canada

Bionique Laboratories, Inc.
Saranac Lake, New York

BioPolymers, Inc.
Farmington, Connecticut

Biotech Research Laboratories, Inc.
Rockville, Maryland

BioTechniques, Inc.
Natick, Massachusetts

Bio-Technology General
Corporation
New York, New York

Biotherapeutics, Inc.
Franklin, Tennessee

B. Braun Biotech, Inc.
Bethlehem, Pennsylvania

Bristol-Myers Company
Syracuse, New York

British Embassy
Washington, D.C.

Brunswick Biotechnetics
San Diego, California

Burroughs Wellcome Company
Research Triangle Park,
North Carolina

E.R. Butts International, Inc.
Bridgeport, Connecticut

CDC Life Sciences, Inc.
Toronto, Ontario
Canada

California Interagency Task Force
on Biotechnology
Sacramento, California

Cambridge BioScience Corporation
Worcester, Massachusetts

Candace Lane Corporation
Parsippany, New Jersey

Celgene Corporation
Warren, New Jersey

Cel-Labs Pty. Ltd.
Manly Vale, NSW
Australia

Celltech Limited
Slough, Berkshire
United Kingdom

Cellular Products, Inc.
Buffalo, New York

Centocor, Inc.
Malvern, Pennsylvania

Charles River Biotechnical
Services, Inc.
Wilmington, Massachusetts

Chembiomed Ltd.
Edmonton, Alberta
Canada

Chesapeake Biological
Laboratories, Inc.
Baltimore, Maryland

Chiron Corporation
Emeryville, California

CIBA-GEIGY Corporation
Summit, New Jersey

Cistron Biotechnology, Inc.
Pine Brook, New Jersey

City of Hannover
Federal Republic of Germany

Commonwealth Serum
Laboratories
Parville, Victoria
Australia

Connaught Laboratories, Inc.
Swiftwater, Pennsylvania

Consulting Statisticians, Inc.
Wellesley, Massachusetts

Coopers & Lybrand
Washington, D.C.

Coors BioTech Products Company
Westminster, Colorado

CuraTech, Inc.
Hauppauge, New York

CyberFluor, Inc.
Toronto, Ontario
Canada

Cytogen Corporation
Princeton, New Jersey

Cytotech, Inc.
San Diego, California

Davy McKee Corporation
Chicago, Illinois

Deloitte Haskins & Sells
San Diego, California

DIAGEN Gmbh.
Dusseldorf
Federal Republic of Germany

Diagnostic Products Corporation
Los Angeles, California

Dynal, Inc.
Great Neck, New York

Ecogen, Inc.
Langhorne, Pennsylvania

Elanex Pharmaceuticals, Inc.
Bothell, Washington

Embryogen, Inc.
Athens, Ohio

Endotronics
Coon Rapids, Minnesota

EniChem Americas, Inc.
Monmouth Junction, New Jersey

Enterovax, Ltd.
Adelaide, S.A.
Australia

Environmental Diagnostics Inc.
Burlington, North Carolina

Farmos, Inc.
Upper Montclair, New Jersey

Fermenta Animal Health
Company
Kansas City, Missouri

Fidia Pharmaceutical Corporation
Washington, D.C.

Fisher Scientific
Pittsburgh, Pennsylvania

Freshman, Marantz, Orlanski,
Cooper & Klein
Beverly Hills, California

Fujirebio America, Inc.
Fairfield, New Jersey

Genelabs, Inc.
Redwood City, California

Gene Link Australia, Ltd.
Melbourne, Victoria
Australia

Genetic Therapy, Inc.
Gaithersburg, Maryland

Gen-Probe, Inc.
San Diego, California

Gradipore Pty. Ltd.
Pyrmont, NSW
Australia

HOM Consultancy
The Hague
The Netherlands

Hazleton Laboratories Corporation
Herndon, Virginia

Hybritech, Incorporated
San Diego, California

Hygeia Sciences, Inc.
Newton, Massachusetts

ICI Biological Products
Wilmington, Delaware

IDEC Pharmaceuticals Corporation
La Jolla, California

IGEN, Inc.
Rockville, Maryland

Immunex, Inc.
Carson City, Nevada

ImmunoGen, Inc.
Cambridge, Massachusetts

Immunomedics, Inc.
Warren, New Jersey

Incell Corporation
Milwaukee, Wisconsin

Institut Armand-Frappier
Laval, Quebec
Canada

Institut Georges Gamow
Clermont-Ferrand
France

InTek Diagnostics
Burlingame, California

InTek Pty. Ltd.
Salisbury, S.A.
Australia

Interfacial Dynamics Corporation
Portland, Oregon

Interferon Sciences, Inc.
New Brunswick, New Jersey

Intergen Company
Purchase, New York

International Bio-Immune
Systems, Inc.
White Plains, New York

International Bio-Research
Walsrode
West Germany

InterPharm Laboratories, Ltd.
Ness-Ziona
Israel

Invitron Corporation
St. Louis, Missouri

Kincannon & Reed
Vienna, Virginia

KabiGen A.B.
Stockholm
Sweden

Lab-Line Instruments, Inc.
Melrose Park, Illinois

Lasher Associates, Inc.
Millsboro, Delaware

Lehigh University
Bethlehem, Pennsylvania

Mary Ann Liebert, Inc.
New York, New York

Life Sciences, Inc.
Philadelphia, Pennsylvania

Life Technologies, Inc.
Gaithersburg, Maryland

Limburg Investment Bank
Englewood, Colorado

Luning Prak Associates, Ltd.
Plymouth Meeting, Pennsylvania

Marine Biologicals, Inc.
Marmora, New Jersey

Maryland Center for Advanced
Research in Biotechnology
Rockville, Maryland

Medarex, Inc.
Clifton, New Jersey

Michigan Biotechnology Institute
Lansing, Michigan

Microbiological Associates, Inc.
Rockville, Maryland

Monoclonal Antibodies, Inc.
Mountain View, California

Montgomery County Office of
Economic Development
Rockville, Maryland

Morgan Stanley & Company
Incorporated
San Francisco, California

National Bureau of Standards
Boulder, Colorado

NeoRx Corporation
Seattle, Washington

Netherlands Foreign Investment
Agency
New York, New York

New Brunswick Scientific Co., Inc.
Edison, New Jersey

New England Deaconess Hospital
Boston, Massachusetts

The Nitragin Company
Milwaukee, Wisconsin

North Carolina Biotechnology
Center
Research Triangle Park,
North Carolina

Northern Illinois University
DeKalb, Illinois

Nova Pharmaceutical Corporation
Baltimore, Maryland

Novo Laboratories, Inc.
Danbury, Connecticut

Orgenics Ltd.
Yavne,
Israel

OROS Systems, Inc.
Cambridge, Massachusetts

Ortho Biotech Imaging Products
Washington Crossing, New Jersey

Osteotech, Inc.
Shrewsbury, New Jersey

Otisville Biopharm, Inc.
Otisville, New York

Otsuka Pharmaceutical Co., Ltd.
Rockville, Maryland

Pacific Biotechnology Ltd.
Darlinghurst, NSW
Australia

Pall BioSupport
Glen Cove, New York

Pandex Laboratories, Inc.
Mundelein, Illinois

Panlabs, Inc.
Bothell, Washington

Peat Marwick Main & Co.
Burlington, Massachusetts

Penn State Biotechnology Institute
University Park, Pennsylvania

Praxis Biologics
Rochester, New York

ProScience Corporation
Sterling, Virginia

ProtaTek International, Inc.
St. Paul, Minnesota

Qlone, Ltd.
Sherwood, Queensland
Australia

Quadra Logic Technologies, Inc.
Vancouver, British Columbia
Canada

Quality Biologics, Inc.
Camden, New Jersey

Regis McKenna, Inc.
Cambridge, Massachusetts

Repligen Corporation
Cambridge, Massachusetts

Rhone Poulenc Research Center,
Inc.
Savage, Maryland

Ribi ImmunoChem Research, Inc.
Hamilton, Montana

Rorer Biotechnology Inc.
King of Prussia, Pennsylvania

Sandoz Research Institute
East Hanover, New Jersey

Seed & Berry
Seattle, Washington

Seragen, Inc.
Hopkinton, Massachusetts

Serono Laboratories, Inc.
Randolph, Massachusetts

Singapore Economic Development
Board
Raffles City Tower
Singapore
Republic of Singapore

Stearns-Catalytic Division
Philadelphia, Pennsylvania

SUNY Center for Biotechnology
Stony Brook, New York

Sverdrup Corporation
Princeton, New Jersey

Synbiotics Corporation
San Diego, California

Taiwan Development Center for
Biotechnology
Taipei
Taiwan

Thailand National Center for Genetic
Engineering & Biotechnology
Bangkok
Thailand

The 600 Broadway Partnership
Seattle, Washington

Transia
Lyon
France

Triton Biosciences, Inc.
Alameda, California

U.S. Department of Agriculture
Agricultural Research Service
Washington, D.C.

U.S. Department of Commerce
International Trade Administration
Washington, D.C.

United Nations Industrial
Development Organization
Vienna
Austria

University of Illinois
Urbana, Illinois

The Upjohn Company
Kalamazoo, Michigan

Utah State University
Logan, Utah

Vestar, Inc.
San Dimas, California

Wallace International Ltd.
Melbourne, Victoria
Australia

Welsh Development Agency
Princeton, New Jersey

Arthur Young and Company
San Francisco, California

ZymoGenetics, Inc.
Seattle, Washington

Elected Leaders, 1988

ABC is governed by elected officers and directors. In addition to serving on the Board of Directors, ABC's President, President Elect, Vice President, Secretary, Treasurer, Past President and General Counsel function as the Association's Executive Committee. The officers and directors of ABC for 1988 are:

ROBERT J. JUDGE, President • Charles River Biotechnical Services, Inc.

Bob Judge is the Vice President of Operations at Charles River Biotechnical Services, Inc. (CRBS), a Bausch and Lomb Company, located in Wilmington, Massachusetts. CRBS was formed in late 1982 and is a full service bioprocessing center, providing contract production of monoclonal antibodies either through its ascites system or with its *in vitro* OPTICELL™ system, both under GMPs. In addition, CRBS provides contract production of recombinant proteins also within the OPTICELL™ systems. CRBS also provides many of the ancillary tests required for screening of contaminants for mammalian cell lines and the products recovered from these cells. Mr. Judge has held a variety of positions within the Charles River Companies during his 20 years with them. His previous work in the sciences was in the areas of microbiology and mammalian genetics. He is currently responsible for both domestic and international operations.

GRAHAM STRACHAN, President Elect • Allelix Inc.

Graham Strachan is President of Allelix Biopharmaceuticals and Vice President & Commerical Director of Allelix Inc. A Canadian biotechnology company, Allelix is located in Mississauga, Ontario (near Toronto). Involved in the formation of Allelix in 1982, he was the first full time employee as Vice President and Commercial Director, responsible for overall commercial strategy, planning and business development. Prior to Allelix Mr. Strachan was with the Agri-Food Group of John Labatt Limited for fifteen years and moved through the patent and licensing function, technology management and business development. Earlier he was with the European Division of Schering in the patents/licensing area. He is a Chemistry graduate from the University of Glasgow, a qualified patent agent, a Fellow of the Patent & Trade Mark Institute of Canada, and a member of the Licensing Executives Society.

THOMAS WIGGANS, Vice President • Serono Laboratories, Inc.

Tom Wiggans' entire professional career has been in the Pharmaceutical Industry (a third generation pharmacist). He has a B.S. in Pharmacy from the University of Kansas and a Masters Degree in Business Administration from Southern Methodist University. For five years Mr. Wiggans held various sales and marketing positions with Eli Lilly & Co. in Jacksonville, Florida and Indianapolis, Indiana. With Serono since 1980 he has been Marketing Manager, Director of Marketing, Vice President of Sales and Marketing, and Executive Vice President/Chief Operating Officer. In 1986 he was named President and General Manager. The company's employment grew from 20 to 200 during this period, including more than 60 field sales representatives; a recombinant DNA production facility was opened; and sales increased by an average of more than 50% annually. Mr. Wiggans is a member of various professional and industry organizations, has served on Advisory Boards and presented papers in the area of Health Care Economics.

MARTIN NASH, Secretary • Synbiotics Corporation

Martin Nash is Vice President of Synbiotics Corporation where he has responsibility for Strategic Development and Corporate Development. The company was founded in 1982 to exploit monoclonal antibody technology in both diagnostic and therapeutic applications. The particular area of application is anti-idiotypic antibody development, in fields as diverse as veterinary or human vaccines and rational drug design. Mr. Nash has served as Co-Chairman of the California Innovation Network.

(over)

EDWARD A. BARTKO, C.P.A. • Treasurer • Coopers & Lybrand (International)
Ed Bartko is a partner in the Washington, D.C. office of Coopers & Lybrand, where he has practiced since he graduated magna cum laude from Thiel College, Greenville, Pennsylvania. He is a member of the firm's High Technology Advisory Committee and currently serves many small and large publicly owned companies which include a number of companies specializing in biotechnology. Mr. Bartko has served as an instructor or panelist for many SEC-oriented courses for outside organizations, and internal courses at Coopers & Lybrand. In addition, he has lectured on SEC-oriented matters at the Georgetown University Graduate School. He is a member of the D.C. Institute of CPAs and the American Institute of CPAs. He has served as Chairman of the SEC Practice Committee of the D.C. Institute on three different occasions and currently is a member of that Committee.

SAMUEL RONEL, Ph.D., Past President • Interferon Sciences, Inc.
Dr. Ronel is President of Interferon Sciences, Inc. (ISI), a company founded in 1980 as a subsidiary of National Patent Development Corporation. ISI's major markets are pharmaceuticals, diagnostics and biological research products. Major products include pharmaceuticals based on natural and recombinant alpha and gamma interferons and other biological factors. ISI is also involved in a joint project with China's Fudan University to synthesize an artificial chromosome for broad application in plant genetics. Dr. Ronel's advanced degree in natural and synthetic polymers is from the Technion in Israel. He also serves as Vice President of Research and Development for National Patent Development Corporation and President of Hydro Med Science, another National Patent subsidiary.

DIRECTORS

DR. ULRICH ALDAG
DIAGEN GmbH
Dusseldorf
FEDERAL REPUBLIC OF GERMANY
THOMAS A. GLAZE
Monoclonal Antibodies, Inc.
Mountain View, California
DAVID HOLVECK
Centocor, Inc.
Malvern, Pennsylvania

HAROLD R. HUTCHINGS, M.D.
Chembiomed, Ltd.
Edmonton, Alberta
CANADA
ANTHONY F. IRVING
BioEnterprises Pty. Ltd.
Roseville, NSW
AUSTRALIA
FRANK F.C. KUNG, PH.D.
Genelabs, Inc.
Redwood City, California

MICHAEL P. KUREK, PH.D.
BioPolymers, Inc.
Farmington, Connecticut
GEORGE W. MASTERS
Immunomedics, Inc.
Warren, New Jersey
SUSAN SMITH-CHAFFEE
Endotronics
Coon Rapids, Minnesota

BRUCE F. MACKLER, Ph.D., J.D., General Counsel

Bruce Mackler, an attorney and scientist, brings to ABC a strong grasp of the legal and regulatory aspects affecting th biotechnology industry particularly FDA, USDA, EPA, OSHA, import/export, international issues and product liability. He i a partner in Mackler, Cooper and Gibbs, Washington, D.C., a firm representing domestic and foreign clients before U.S. Federa agencies, legislatively and in the courts. He holds a doctorate (University of Oregon Medical School, 1970) in Microbiology/Immu nology and has published over 100 articles in scientific journals.

As ABC General Counsel, he has been instrumental in organizing many of the Association's programs—regional meeting patent office interactions; dialogues with federal regulatory agencies; membership, international liaison; the industry insuranc program; congressional liaison; and the ABC Dialog Column, among others.

Along with these activities, Bruce regularly publishes articles on various biotechnology issues in **Genetic Engineering News BioEngineering News, Biotechniques,** and is Managing Editor of **Biotechnology Law Reports.** He also lectures t biotechnology groups on regulatory and legal matters.

DETAILS

News of Interest to Members of the Association of Biotechnology Companies

VOLUME 4, NUMBER 3 MAY–JUNE, 1988

Inside This Issue...

Congressman Dingell Speaks Out–Influential legislator gives his views on biotechnology, the Government, and industry

More ABC Meetings–ABC plans fall lineup of meetings and schedules Third International Biotechnology Meeting

FDA Compliance Alert–The agency is taking a tougher look at research *in vitro* reagents, and ABC is concerned

New Board Elected–ABC members select new Association leaders

From Capitol Hill–Congress looks at patents, competitiveness, field tests, and more

Berkovitz and Biotech–New Supreme Court product liability decision could result in more caution by FDA reviewers

Corporate Profiles–A look at ABC members Environmental Diagnostics, KabiGen, and Pacific Biotechnology

Biotech and Accounting–Steven Burrill identifies some tricky accounting issues for biotechnology companies

ABC Strengthens Membership Department–Cynthia Waxvik joins the staff

New Mail Regulations–Proposal by Postal Service

New Members–ABC surpasses 175 total members

REMARKS OF THE HON. JOHN D. DINGELL

At the Association of Biotechnology Companies Meeting, March 29, 1988

I am pleased to be here today to address this international meeting of the Association of Biotechnology Companies.

Your industry, and the technology it is based on, represents a scientific revolution which will play an ever more important role in our future. The discoveries and advances we expect in the areas of human and animal health, agriculture and the environment will benefit all of society. There is also the promise of great economic benefits for those companies and entrepreneurs who develop and market new products. By the year 2000, biotechnology-related sales from U.S. companies alone are expected to total $25 billion.

The biotechnology revolution has been a rapid one, in more than one sense. First, many of the bioengineering techniques being used are relatively new, having been developed in the past decade. And second, laboratory ideas can become commercial products in a very short time.

As with all revolutions with broad scientific and economic consequences, the dramatic pace of change brings with it some problems and concerns. For the

(continued on p. 4)

ABC Elects New Officers and Board of Directors

On June 15, members of the Association of Biotechnology Companies (ABC) elected its new officers for 1988-1989. ABC's new President is **Robert Judge**, Vice President of Operations at Charles River Biotechnical Services and President-Elect is **Graham Strachan**, President of Allelix Biopharmaceuticals, Inc., Toronto, Canada.

Elected as Vice President was **Thomas Wiggans**, President of Serono Laboratories, Inc.; as Secretary, **Martin Nash**, Vice President of Synbiotics Corporation; and Treasurer, **Edward Bartko**, Partner, Coopers & Lybrand (International).

The following new ABC Board members were elected for three year terms: **Susan Smith** (Endotronics), **Dr. George Masters** (Immunomedics, Inc.), **Dr. Frank Kung** (Genelabs, Inc.), and **David Holveck** (Centocor, Inc.).

MARK YOUR CALENDAR...

ABC's 1989 International Biotechnology Meeting

The Third International ABC Biotechnology Meeting is scheduled for March 29-31 at the Park Hyatt and Westin Hotels in Washington, D.C. The three-day Spring meeting will

(continued on p. 5)

FROM CAPITOL HILL

by Sue Moreland, Director of Communications

The upcoming presidential conventions have dampened the momentum for Congressional actions. In the months before November, elected officials will focus their attention on appropriations, high press/public profile legislation, and their own campaigns.

However, two legislative packages, the Rose/Hatfield bills to ban animal patents and Baucus' environmental release bill, offer the media hype sought by lawmakers. These two bills jeopardize the current regulatory climate which does not differentiate products based on the manufacturing process.

SHOULD A PRECEDENT BE SET FOR DISCRIMINATING AGAINST PRODUCTS BASED ON ALLEGED MORAL OR ETHICAL ISSUES, NOT SCIENTIFIC ONES? THAT IS THE QUESTION CONFRONTING THE CONGRESS AS TWO COMMITTEES CONSIDER THE PATENT AND ENVIRONMENTAL RELEASE BILLS.

Patent Act: The Rose Amendment

"Once animal patents are stopped ... the next target will be plant patents ... then the *Chakrabarty* decision," proclaimed a member of Rifkin's anti-transgenic animal coalition recently.

The legislative debate surrounding H.R. 3119 (Rose) and S. 2111 (Hatfield) has shed the narrow focus on animal patents. The anti-biotechnology coalition has expanded into the areas of government supported biotechnology research, whether regulations are adequate, and whether industry should be allowed to "commercialize Mother Nature."

Status: H.R. 3119 (the Rose Amendment): Markup is pending in the House Judiciary Committee, Subcommittee on Courts, Civil Liberties, and the Administration of Justice. At this time, if voted upon by the Subcommittee members, the Rose bill would pass. ***ABC staff and Steve Holtzman,*** COO for **Embryogen,** met with Committee Chairman Kastenmeier to express the industry's opposition to H.R. 3119.

Following that meeting, Chairman Kastenmeier organized a meeting with Henry Waxman (D-CA, chairman of the Subcommittee on Health and the Environment), James Scheuer (D-NY, chairman of the Subcommittee on Natural Resources, Agriculture Research and Environment), Tom Foley (D-WA, Majority Leader), and Charlie Rose to discuss political ramifications from passage of H.R. 3119.

The attendees concluded that if H.R. 3119 escaped from the Judiciary Subcommittee, the animal welfare advocates, the environmentalists, the religious groups, the farmers and Rifkin's allies would have a field day creating public panic about the emerging biotechnology industry.

By emphasizing the important medical and nutritional strides bio-engineered animals offer, **ABC succeeded in refocusing the Congressional debate** from a fear of the "mega-pig" to one of how such animals may be used to benefit society.

Senator Edward Kennedy (D-MA, Chairman of the Committee on Labor and Human Resources) has gone on record opposing S. 2111 (Hatfield's bill). "It would be improvident to retard the development of this emerging technology which holds such great promise to contribute to our nation's health and economic competitiveness," he said

Baucus (D-MT) "Novel and Exotic Organism Release Act"

This legislation preempts existing legislation, consolidating regulation of environmental releases under the Toxic Substances Control Act (TSCA). Draft language in the bill is extremely broad. Many provisions are troublesome, and ABC has informally conveyed its concerns to staffers.

Status: Scheduled to be introduced shortly.

Product Liability

ABC supported the section in the unamended H.R. 1115, the Uniform Product Safety Act, providing limitation of liability (punitive damages) if a product has been approved by the federal regulatory agencies. However, the bill has been seriously damaged by an amendment, which the Association opposed, exempting any drugs which affect implantation of an egg into the uterus (such as contraceptives).

Status: Consideration of H.R. 1115 is scheduled to be completed by the House Energy and Commerce Committee. The bill will then be referred to the House Judiciary Committee. The product liability bill has been highly controversial over the years and the outlook again looks bleak.

Food Safety Bill

On June 6, Senator Orrin Hatch (R-UT) introduced bill 52468 which preempts States from setting requirements for food additives different than those set by the Food and Drug Administration, substitutes a "de minimis policy (negligible risk)" for the Delaney Clause, and authorizes $10 million for biotechnology demonstration projects.

Business Taxes

On April 22, Senators Baucus (D-MT) and Danforth (R-MO) introduced S. 2312, the Entrepreneurs' Research Incentive Act. This bill amends the Internal Review Code of 1986 to make the research credit available to certain start-up ventures.

Chiles' Biotechnology Competitiveness Act, S.1966

(continued on p. 3)

This legislation establishes a forum for U.S. strategic planning in biotechnology, a national advisory panel on the human genome, and a national center for biotechnology information.

Status: S.1966 was approved by the Senate on June 17th. An amendment [Leahy D-VT)] to authorize the establishment of a **National Project to Map Plant Genomes,** was also included in the easily passed bill. ABC supported this amendment.

Status: On July 17th, ABC will be presenting testimony before Congressman Scheuer's subcommittee on S.1966 and H.R.4502.

Intellectual Property Bankruptcy Protection Act

Under current law, if a technology licensor goes bankrupt, the bankruptcy trustee may rescind all the license agreements. S.1626 (Senator DeConcini (D-AZ)) AND HR4657 [Representative Edwards (D-CA] have been introduced to eliminate this problem. The bills revise the Bankruptcy Code to prevent bankruptcy trustees from interfering with the rights of the licensees.

Status: Hearings have been held on both bills. Markup should be scheduled by the Senate Judiciary Committee for the week after the 4th of July recess.

Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)

This bill, S.1516, reauthorizes the federal pesticide regulatory program. As a result of ABC's efforts, it incorporates a Congressional mandate " [To study] the potential contributions of biotechnology to reduce domestic reliance on, and human exposure to pesticides. "

Status: Reported by Senate Agriculture Committee May 4, referred to the Judiciary Committee, May 19. There is not a companion bill in the House.

Corporate Profile: KabiGen AB

KabiGen AB is a research and development company specializing in genetic engineering and cell biology. The company's main business is contract research work, centered around pharmaceuticals and animal vaccines. The company also develops processes, techniques and products for licensing, mainly to the pharmaceutical industry.

A complete genetic engineering and cell biology company, KabiGen is a subsidiary of KabiVitrum AB, and a member of the Procordia Group, Sweden. KabiGen was established in 1978 by the then Kabi AB and Statsforetage AB, in order to exploit the new techniques of genetic engineering. That same year, KabiGen signed one of the first genetic engineering contracts in the world with Genentech, Inc., covering the development of a microorganism which could produce human growth hormone, hGH. This hGH is currently marketed by KabiVitrum.

KabiGen's first molecular biology laboratory came into operation in 1981, after public doubts in Sweden on the production of proteins and peptides by genetic engineering had been resolved. KabiGen has subsequently developed into a genetic engineering company with the expertise necessary to pursue projects all the way from molecular biology to pilot-plant production and protein purification.

Research at KabiGen is concentrated in two main areas: peptide hormones and peptides; and products which regulate blood coagulation and fibrinolysis.

Peptide hormones and peptides are produced in a process known as the EcoSec System; this is an E. coli expression system in which the product is secreted directly into the surrounding culture medium as a fusion protein, then cleaved to release the free peptide.

During 1987, KabiGen started to market the EcoSec System worldwide. In April 1988 a licensing agreement was signed with Genentech, for the production of Insulin-like Growth Factor I (IGF-I). (See March-April *DETAILS.*)

A further development and application of the EcoSec System is the manufacture of subunit vaccines. KabiGen has produced a number of vaccine components for animal health companies and these components are now being tested and evaluated.

KabiGen is also working on tissue-specific Plasminogen Activator (tPA and has developed "second-generation" tPA variants which have longer half-lives and are more active than native tPA. In addition, KabiGen is developing a mammalian cell line for the production of Factor VIII.

KabiGen has in-house fermenters up to 75 L in volume in specially-designed laboratories, as well as complete facilities for pilot-scale protein purification and analysis. Eight bioreactors are available, ranging in size from 2 L to 75 L. All are used exclusively in agitation and cell recirculation, as well as methods for the total exclusion of cells from effluent lines.

The process development group has experience with different types of micro-carriers, including optimization of protocols for propagation; passaging; relation of type of carrier to cell; minimization of shear forces; and the high density culture of anchorage-dependent cells.

For more information, contact Dr. Roger Bishop, Marketing Manager, Stockholm.

REMARKS, *cont. from p. 1*

burgeoning biotechnology industry to reach its full potential, those issues have to be addressed carefully, thoughtfully–and quickly.

Unfortunately, this Administration and the Federal research and regulatory agencies have thus far failed to focus the appropriate attention and resources on biotechnology. And, to be fair, Congress has also often failed to look at biotechnology from the proper perspective, dealing only with the isolated problem areas.

In my judgment, we need to see biotechnology in the greater context of U.S. competitiveness in science, technology and trade. And against that background, the major problems Congress must address — in the absence of effective national leadership–become clear.

Let me take them in turn.

First, there must be continued Federal support for research and development.

The good news is that America is the world's leader in biotechnology innovation. But we were also once the world's leader in steel, in shipping, in electronics, and a host of other sectors. We can't take our position for granted.

Our greatest trade rivals are devoting enormous resources to obtaining equality in this area. Countries like Japan, France, The United Kingdom and West Germany have initiated national research programs promoting biotechnology. At the same time our own Administration has continued to attack funding and staffing levels at the National Institutes of Health. To maintain its leadership, America must be willing to support research and training with the funds these vitally important activities deserve.

American scientists are the best researchers in the world, but too often we have lost control over technological innovation. There is a big gap between the petri dish and the production line. Our competitors make that transition very well. We must do better, by supporting applied research. Instead of selling off the NIH to the highest bidder, we need to develop a long-term research and development agenda for the future. We must show the necessary foresight to protect and move forward with our scientific knowhow and to capitalize on our research investments.

Second, we need to untangle America's system for regulating biotechnology.

What has happened with the regulation of biotechnology products is that old statutes have been massaged to fit new technologies and new products. Frankly, the fit is not very good. The current system is cumbersome and inefficient, with overlapping responsibilities among the regulatory agencies, and inappropriate exemptions.

What we must do, and do soon, is sort out the regulatory mess. The public needs to know that health and the environment will be protected, while industry needs a fair and predictable regulatory system with clear guidelines. If the technology proceeds without an adequate regulatory framework, it will become mired down in public opposition and law suits.

I addressed these issues in hearings in 1984 and 1985. I am concerned that little has changed since then, and that the competitiveness of our biotech industries is suffering as a result.

That brings me to a related point. *We need to harmonize regulations and standards at the international level.*

We must strive to ensure that the international playing field is a level one, free of inappropriate barriers to trade, and with adequate protection for intellectual property.

This is never easy, but there are some encouraging signs. The rest of the world is also wrestling with these issues, and other countries look to America for advice and guidance. The U.S. role in organizations like the OECD is important. But before we tell other people how to conduct their affairs, we first have to get our own house in order.

At the GATT talks, for the first time a multilateral trade negotiation has seen intellectual property as a trade issue. The recognition is a breakthrough for the biotechnology industry, but there is a long way to go before standards are finally written down on paper.

The U.S.-Canada Free Trade Agreement contains a chapter on the harmonization of technical standards related to health, safety, the environment and production processes, to prevent such standards from being used as barriers to trade. Elsewhere in the agreement the parties are required to work towards harmonizing health and safety requirements for veterinary drugs, pesticides, and the packaging, labelling and inspection of foods.

These beginnings are encouraging. Less encouraging is the lack of action by our own Department of Commerce. There have been few substantive initiatives from Commerce in the area of biotechnology. In fact the Department seems to be at war with itself. On the one hand, they're counting on future profits from biotech industries to reduce our massive trade deficit. On the other hand, they're considering a number of export controls on biotechnology. There is no clear leadership here, and as a result, our industries suffer.

(continued on p. 5)

That brings me to my final point: we need to nurture and protect our scientific ideas and products.

This means that the patenting issues which biotechnology presents must be resolved. If the patent system needs to be changed, then let's find out what needs to be done and then do it. We can't muddle through any longer. Furthermore, we must clear the backlog of biotechnology-related patents which is currently sitting at the Patent and Trademark Office.

We must also support small biotech firms in this country. These firms are in many cases the catalysts for technological advances. Too often such firms–rich in ideas but short on capital–are bought up by larger corporations. Foreign investors also shop around for these small firms, buying ideas and innovations.

I am not arguing for restrictions on the flow of information and ideas into and out of this country. But I am arguing that we ought to do something to stem the disturbing and accelerating trend of American ideas being transformed into marketable products made overseas by foreign companies.

Let me conclude with a final thought. The areas I've discussed this morning–research, regulation, and protection —are by no means the only issues involved in the continued development of biotechnology. But they are some of the major issues that Congress should put on the public agenda, and they are a few of the issues that we can do something about.

The pace of change in biotechnology is only going to accelerate. The sooner we can resolve these problems, the better. I'll give you my word that I'll do everything within my power to help resolve them–but I'll ask in return that you help me and my colleagues in the Congress who want to see us realize the promise of biotechnology.

Then America, and the rest of the World, will receive the benefits that the biotechnology revolution has to offer.

MEETING, *cont. from p. 1*

bring together even more biotechnology executives, government officials and regulators, and international delegations representing companies and government bodies, than attended ABC'S successful two-day meeting this year. The 1989 International Meeting willl emphasize worldwide commercial opportunities and seek to maximize opportunities for interaction. ABC already has commitments for Australian, United Kingdom and Canadian biotechnology industry sessions.

The affinity discussion groups (initiated this year) will be expanded, ABC Committees and President's/ CEO's will again meet informally for breakfast, and a variety of plenary, roundtables and workshops will take place with an Embassy Reception to round out the program. Additionally, consultation booths (an area to hold private business discussions), will be available as well as information tables for use by member companies and attendees participating in Affinity Groups.

Complementing the successful program format for ABC's annual meeting, the 1989 meeting will offer some unique new features. A group of ABC's Council of State Biotechnology Centers will organize a one-day session during the meeting. Also, the Biotechnology Purchasing Managers Association (BPMA), a group of approximately 150 purchasing executives, plan to host their annual meeting concurrently with ABC. As ABC and BPMA develop their programs, some sessions and activities will be held together, while others will be hosted separately.

ABC'S FALL LINEUP

A series of educational programs are being organized for October. To be held both on the East Coast and the West Coast, the one-day programs will be scheduled to minimize cost and maximize value for biotechnology executives.

TENTATIVE DATES AND LOCATIONS:

Biosafety: Oct. 5, Boston; Oct. 19, New Jersey.

Biostatistics: Oct. 4, Boston; Oct. 26, San Francisco.

Manufacturing and Quality Controls for Biotechnology Products: Oct. 18, New Jersey; Oct. 26, San Francisco; Oct. 28, San Diego.

Design and Construction of Biotechnology Facilities: Oct. 4, Boston; Oct. 18, New Jersey; Oct. 28, San Diego.

Medicare Reimbursement for Biotechnology Products: Oct. 4, Boston.

1988 Regulatory Update and Issues: Oct. 5, Boston; Oct. 27, San Francisco; Oct 29, San Diego.

Biotechnology Company Management Structure, Compensation and Employee Issues: Oct. 5, Boston; Oct. 19, New Jersey; Oct. 27, San Francisco; Oct. 29, San Diego.

Four primary locations are being considered--Boston, New Brunswick/Princeton, San Francisco and San Diego. Most of the programs will be held more than one time, for instance, Biostatistics in Boston and San Francisco or Design and Construction in Boston, New Brunswick/Princeton and San Diego. Watch for further details in July, and/or call Jean Mills at ABC Headquarters.

Financial and Accounting Issues Affecting Biotech Firms

G. Steven Burrill

From start-up to success as fully integrated entities, biotechnology companies face a wide range of financial and accounting issues. Until recently, biotech companies were challenged primarily by their need to find capital for funding research and development. As they progress into the commercial marketplace, biotech companies are facing new challenges–financing new activities such as manufacturing, market development, and the creation of sales organizations. At all stages of development, the accounting choices biotech companies make influence the business strategies they employ later on.

IN THE R & D PHASE

Until recently, the public equity markets were receptive to biotech's initial offerings and provided a strong source of capital–even for companies that lacked marketable products. However, since October, biotech companies have been looking for financing alternatives. They are turning once again to limited partnerships to fund research and development. They are also forming strategic alliances, quite often with foreign investors whose investment philosophies are compatible with biotech companies' long-term growth patterns.

IN THE PIPELINE

As products–especially therapeutics–near production, biotech companies must plan for the expenses and delays frequently associated with clinical trials and manufacturing costs. Clinical trials are time-consuming and therefore costly. Genentech's experiences with FDA rulings on TPA illustrate the importance of having sufficient capital through the trial stages. Companies must sustain themselves until products in the pipeline reach the market and begin generating revenues. Strategic alliances play an increasingly important role at this stage of company development. Strategic partners can provide a manufacturing and marketing infrastructure, as well as capital, in exchange for access to innovative technology.

In our experience, many biotech company executives worry–perhaps needlessly–about financing the high costs of establishing manufacturing facilities. Depending on the product in development, gearing up for manufacturing may not be as expensive as feared. For instance, if the drug is potent enough that small quantities of it will meet market needs, then the facility may not be as expensive as is necessary were the company producing tons of fertilizer or aspirin. Accounting for these costs can be rather complex, involving concepts such as inventory accounting and methods, costs capitalized, obsolescence, lower of cost or market considerations, etc.

Selecting the most advantageous method of accounting for the vast research development expenditures is crucial to the company's ultimate success. Initially, the company has definitional questions. What is research and development? Does the cost of R & D include certain overhead and indirect costs? What about the cost of clinical trials and the creation of certain tangible development assets?

Having agreed to a working definition, the company must decide how and when to capitalize or expense the costs associated with R & D for tax purposes (alternate methods are permitted). As creative funding approaches have appeared, so too have interesting accounting problems resulted from the need to properly match costs with applicable funding, given the legal considerations of who bears what risks.

Additionally, young companies must also assume the costs of protecting their technology through patents. Our survey, "Biotech 88, into the Marketplace," suggested that young companies did not consider obtaining patents to be a top priority. However, the litigation between biotech companies emphasizes how instrumental patents are in securing future marketing rights.

Companies must plan to protect their technology from the very beginning, which may mean eventually defending patents through legal action, if necessary. Patents are effective to the extent they can be defended, and companies of all sizes can incur substantial legal fees in protracted court battles. Accounting for these expenditures either as expenses or as deferred costs is an issue. If the expenditures are deferred, how and when they are written off becomes a further complication.

IN THE MARKETPLACE

Ideally, as integrated and mature entities, biotech companies will rely on sales revenues to generate the capital they need. Product revenues will fund new research and development efforts, from which new products derive. This is the hope and the ultimate commercial goal of the industry. The extent to which this dream is realized will depend to a degree on the kinds of strategic alliances, and consequently the licensing arrangements, companies have made with other partners. If a company has "licensed away" its technology, the profits it realizes will be smaller than if it owned the proceeds outright. Nevertheless, a block-buster product has the potential to generate so much money for a company that even a percentage of the total returns can make a substatial contribution to company operations. Determination of revenue recognition methods and timing are critical here, and tax and accounting rules are usually different.

Accounting for the biotech industry is evolving rapidly.

(continued on p. 7)

Revenue and expense items that frequently occur in this evolution need to be and are accounted for in non-traditional ways. This "non-traditional approach" to accounting results from the need to best match timing requirements, risk/reward relationships, and the standards set by two entirely different rule books–generally accepted accounting principles and the Internal Revenue Code.

G. Steven Burrill is Chairman of the National High Technology Group for Arthur Young.

ABC RE-ORGANIZES ITS COMMITTEES

Miss Cynthia Waxvik, the new Assistant Director of Membership Services, has been re-organizing the ABC committee structure. Operational now are several committees with chairpersons actively building upon the decisions and recommendations made at committee breakfast meetings during the ABC International Meeting in March. ABC members interested in serving on any of these committees should contact Miss Waxvik:

Agriculture and the Environment Committee - Mel Bauk
CEO/President Committee - Thomas Wiggans
Education Committee - Chris Lowell
Financial Management Committee - Edward Bartko
Manufacturing/Operations/Production Committee - Michael Paulix
Marketing/Business Development Committee - Susan Smith
Regulatory and Patent Affairs Committee - Kenneth Graziano
Research and Development Management Committee - Samuel Ronel

To facilitate interactions, ABC will rely on telephone conference calls to among committee members.

From The General Counsel's Desk:

FDA COMPLIANCE ALERT

FDA has recently taken a more aggressive attitude toward what it perceives as excessive sales and distribution of investigational Class III *in vitro* diagnostic devices. Apparently, FDA is concerned that biotech companies are treating such sales almost as full-fledged commercial opportunities prior to FDA premarket approval for these investigational devices.

Local FDA District Offices have stepped up visits to clinical laboratories to identify investigational products being used for diagnostic tests. Based on such findings, FDA has sent Regulatory Letters to Wang Laboratories and Coulter Corporation. Both companies, under extreme FDA pressure, have adopted the use of physician cards, first required in the Centocor Consent Decree. Individuals ordering investigational diagnostic tests must sign a statement acknowledging that they understand the device purchased or test ordered is an investigational (or research) product, not for *in vitro* diagnosis or therapeutic use. Unless the card is signed, further shipments are barred.

ABC encourages its members to adopt a proactive policy. First, biotech firms–particularly those with Class III investigational devices– should warn in their informational documents, package inserts, newsletters, and sales documents reminding purchasers that the investigational or research items are not for diagnostic use. Second, where firms become aware of such use, it should send a reminder letter to the user stating that these products are for research or investigational use, and not for clinical diagnostic use. Third, firms should periodically review their customer lists to see if any reference or clinical laboratories who do not do research are present; then send them a reminder letter.

FDA intends to aggressively recommend that biotech and traditional firms adopt the user acknowledgement statement procedure. ABC believes that such a requirement is beyond FDA's statutory power, economically burdensome, especially to smaller firms (estimated cost $35,00 - $50,000 per year) and unwarranted. Biotech companies can only rely on the representations of its customers and cannot become surrogates of the FDA and inspect their customers' use of products.

Unable to influence clinical laboratories, which are not subject to FDA regulation, the Agency seeks to pressure biotech firms to restrict sales of investigational and research products. ABC believes these efforts are misdirected. The FDA should be encouraged to educate clinical laboratories through their associations, direct mailing and workshops regarding their concerns. FDA should not place the burden on the biotech and traditional device manufacturers.

ABC members interested in forming a working group to deal with this problem should contact Bruce F. Mackler. Companies can participate directly or indirectly in the working group. ABC would like to put together a delegation of biotech companies to meet with FDA personnel and impress upon the Agency ABC's concern over this new policy.

Bruce F. Mackler

CORPORATE PROFILE: ENVRIONMENTAL DIAGNOSTICS

Since 1983, Environmental Diagnostics, Inc., Burlington, North Carolina, has developed, manufactured and marketed its proprietary diagnostic and screening tests which are used to detect substances in foodstuff, animals, humans or the environment that may be hazardous to human health.

The EZ-SCREEN System developed by EDI incorporates certain immunoassay techniques to provide a high analytical accuracy and specificity. The EZ-SCREEN System consists of the QUIK-CARD, all reagents (chemicals) necessary to perform the test and disposable pipettes packaged in a blisterpak format (about the size of a deck of playing cards). The QUIK-CARD is essentially a "sandwich" of filter material placed between layers of plastic and vinyl labeling. The filter material and plastic portions are engineered to allow automated assembly and to control flow rate precisely. Antibodies specific to the analyte are applied, and the analyte is trapped and "focused" at the reaction site by the antibodies.

Reagent stability is increased in the EZ-SCREEN System by the use of bicomponent packaging. Lyophilized or dry components are physically separated from liquid components in the reagent vials by the use of ampules enclosed within the outer vial. The dry components are rehydrated by crushing the ampule in the vial just prior to performing the test, thus yielding a "fresh" solution for test performance. Typically the entire test process can be completed in 10 minutes or less.

As a result of this unique format, the EZ-SCREEN System has the following performance characteristics and features:

- test capability in non-laboratory settings
- high sensitivity
- inexpensive compared to conventional laboratory tests
- accuracy comparable to laboratory tests
- simple to use, can be operated by non-technical personnel
- portable, no instrumentation required
- can be used to detect a wide variety of substances
- multi-test format capability

Currently, EDI produces QUIK-CARDS with two, three, or six ports. Each port is used as a test site or control site. Three port cards can be used to test two field samples or to include both a positive and a negative control (this procedure is used for drugs of abuse tests). Six port cards allow multiple sample testing or tests for several substances at one time. Other multi-port configurations can be produced to meet customer requirements in specific markets.

As a result of this versatility, the EZ-SCREEN Systems has applications in several emerging markets, including agridiagnostics and environmental testing, in addition to the established market for clinical diagnostics. Together, these are the three target markets identified by EDI for its product development activities. EDI currently has 8 tests available for commercial sale in these markets.

For further information, contact **Heather Hand-Ruger**, Director of Administration.

LETTER TO THE EDITOR

The article entitled "Dutch Cost-Containment Affects Fair Market Price for Biotech Products" in the March/April DETAILS inaccurately stated the impact of the new Dutch reimbursement policies on the sizeable biotechnology industry in the Netherlands.

The Dutch Government has, within the framework of a total cost-containment policy for its national health insurance plan, proposed controlling the price levels of drugs and biologics–a step similar to discussions being carried on in other countries, such as the Federal Republic of Germany. In this respect it is important to know that The Netherlands currently has the highest prices in Europe for these products, a point omitted from your article.

In summary, the new Dutch proposals cover the creation of a price system for drugs and biologics based on comparison with a price range of identical or therapeutically equivalent products being sold within The Netherlands. Because biotech products are unique, this new pricing is expected to have little influence on the price of biologics, as there will be no alternative drugs on the market. This minimizes the impact on the Dutch biotech industry.

Within the framework of Europe 1992, the EC is discussing measures that will increase the transparency of drug/biologic prices.

Willem Thone
Netherlands Foreign Investment Agency

ABC STRENGTHENS MEMBERSHIP SERVICES DEPARTMENT

As part of ABC's continuing program to improve membership services, **Cynthia Waxvik** joined ABC on June 8th as the Assistant Director of Membership Services.

In this role, Miss Waxvik will focus on identifying and providing membership services. She will also help establish ~~five~~ technical standing committees (see page 7 "ABC Re-Organizes..."); Marketing/Business Development; Manufacturing/Operations/Production; Regulatory/Patent Affairs; Research and Development Management; and Financial Management.

Miss Waxvik will also be organizing regional ABC chapters, and fielding member's questions about the committees and ABC services. When asked about her goals, Ms. Waxvik commented, "I see a tremendous opportunity to expand the services ABC offers its members. I am looking forward to meeting our members and developing creative ways to meet their needs."

Before coming to ABC, Miss Waxvik worked with an international security association in the meetings and seminar department. She produced international conferences, designed membership campaigns, and developed committees.

A native of North Dakota, Miss Waxvik has a B.S. in Chemistry and a Masters of Association Management degree from George Washington University. She has also been highly involved in the formation and establishment of the Masters of Association Management program.

TWO DAY AUGUST CONFERENCE

Sydney, Australia

The Australian ABC Chapter together with the Australian Government has organized the **Commercial & Regulatory Aspects of Biotechnology - An International Perspective Conference**, August 30-31, 1988, in Sydney, Australia. The Conference will focus on international commercial opportunities, strategies and competitiveness in biotechnology. Dr. Robert Yuan, author of the U.S. Governmental studies entitled *Biotechnology in Western Europe* (1987) and *Biotechnology in the Pacific Rim* (1988), will focus on commercial biotech and government support strategies in Asian Countries, Japan, U.K. and The Netherlands. Dr. Mark Dibner, author of *Biotechnology Guide USA: Companies Data and Analysis* (1988), will provide a detailed analysis of U.S. licensing, joint-ventures and partnerships with non-U.S. firms.

Other speakers include ABC members from the Australian biotech industry with hands-on experience in negotiating international commercial agreements, licenses and joint-ventures. Australian and U.S. governmental speakers will provide insights into trade and commercial policies, as well as product registration requirements.

ABC members interested in having their corporate information literature distributed at this Australian Conference to Australian biotech companies should contact Bruce F. Mackler, ABC General Counsel. ABC will have literature tables available to facilitate interactions between companies.

GERMAN DRUG LAW AMENDED AFTER INDUSTRY OUTCRY

The Regulations for Pharmaceutical Entrepreneurs enacted by the Bundersrat February 26, 1988, amended the prior German diagnostic device regulation. ABC had complained to the U.S. and German governments about this regulation. Effective January 1, 1989, the amended law made the following changes which industry had requested:

1. single components of diagnostic kits are exempted from the labeling provisions of the law; outer cartons of single components must have lot numbers, active ingredients and any necessary information;

2. actual expiration dates are again acceptable, not the June 30th and December 1st requirements of the prior law; and

3. retention samples for products are now related to shelf-life of the product: e.g., 3 months retention for products with shelf-life less than 3 months, 6 months retention for a 3 - 12 month shelf-life product.

ABC now has up-to-date copies of "Implementation of GMP in the Federal Republic of Germany." This document is available to its members for the cost of photocopying and mailing ($25.50). For copies send a self addressed label and check to ABC Documents, Association of Biotechnology Companies, 1120 Vermont Avenue, Suite 601, N.W., Washington, D.C. 20005; no telephone orders.

BERKOVITZ & BIOTECH

By Jeffrey N. Gibbs

On June 13, the Supreme Court decided a product liability case of potentially great significance to the biotech industry. The Court unanimously and firmly held that FDA could be sued for injuries to patients that result from FDA's negligently failing to follow a course of action set in a statute, regulation, or policy.

The case began with the vaccination of 2 month-old Kevan Berkovitz against polio. According to the lawsuit, Kevan contracted polio, which resulted in almost complete paralysis. The Berkovitzes sued Lederle, the manufacturer of the vaccine, and FDA. After settling with Lederle, the Berkovitzes continued their suit against FDA.

In *Berkovitz*, the plaintiff alleged that FDA had violated its regulations in two respects: by licensing Lederle's polio vaccine, and by approving the particular lot that Berkovitz had received. The agency argued that those actions involved a "discretionary function." Under U.S. law, the Government cannot be sued for discretionary functions. Thus, said FDA, it should be immune from suit.

The Court disagreed. The Berkovitz complaint alleged that FDA had failed to demand certain data specifically required by its regulations before licensing the product. That allegation was found to be sufficient. FDA "has no discretion to issue a license without first receiving the required test data; to do so would violate a specific statutory and regulatory directive." The Court also held that FDA could be found liable if it had "knowingly approved the release of a lot that did not comply with safety standards."

The Court's ruling does not mean that FDA is liable for Kevin Berkovitz' injuries. The ultimate issue of negligence still remains to be decided. It does mean, though, that the plaintiff will have a chance to prove his allegations.

It is far too early to assess the impact of *Berkovitz* on the biotech community. The likelihood, though, is that federal agencies will become more cautious in reviewing product applications. To a large extent, the Court's ruling may mean that FDA, EPA, and USDA will feel vulnerable if they do not dot every "i" and cross every "t". If a regulation says that certain data must be submitted, then agencies may look doubly closely to see that each item has been included in the application. Regulation by check-list could proliferate. The agencies may also be less willing to waive data requirements, for fear that it will be considered a breach of their duty. These developments would slow product reviews.

At the same time, agencies might show greater preference for broader, vaguer guidelines. Documents such as the biotech Points to Consider may leave the agency less vulnerable to suit. It was the specificity of the FDA licensing and release regulations that led to the Court's ruling. Preserving discretion becomes critical to a successful "discretionary function" defense.

For more information about *Berkovitz*, contact **Jeffrey Gibbs**, ABC Associate General Counsel.

POSTAL SERVICE PROPOSES NEW MAIL REGULATIONS

On June 24, the U.S. Postal Service proposed a complete ban on the mailing of "etiologic agents." 53 *Federal Register* 23775. For many years, the Postal Service has allowed the mailing of etiologic agents, if they were properly labeled and packaged. If the proposal is adopted, however, no company or researcher could mail any "viable microorganisms or their toxins which cause, or may cause, human disease."

The Postal Service gave only a cryptic explanation for this abrupt change in policy. It said that it had "learned that some customers propose increased use of the mails to transmit etiologic agents. . . . Mailings of etiologic agents in such numbers might present a hazard to postal workers and to the public."

ABC believes that the change is unwarranted, and based entirely on emotional fears. Significantly, the Postal Service cited only a potential hazard, not any actual incidents. Even if the change would have only minimal practical significance, ABC is concerned by the precedent established and the lack of a justification for this change.

Comments on the proposal are due by August 8. For more information, contact Jeffrey Gibbs.

CORPORATE PROFILE: PAC BIO

Located in Sydney, Australia, Pac Bio (Pacific Biothechnology, Ltd.) is the first commercial enterprise closely aligned to a leading research institute (the Garvan) that is situated on the campus of a major medical teaching hospital (St. Vincent's Hospital, Sydney).

To achieve its status as an integrated Australian biopharmaceutical company of international standing, Pac Bio is:

- focusing research on diseases with a high potential for significant therapeutic gains;
- optimizing opportunities for interaction between basic research (the Garvan), applied research (Pac Bio) and modern clinical practice (St. Vincent's);
- developing its own marketing capacity in Australia and Asian territories and working through a network of close international corporate relationships in North America, Europe and Japan;
- licensing in, or forming marketing alliances for, new products being developed in the biopharmaceutical industry.

Pac Bio is a joint venture between California Biotechnology, Inc.; the Garvan Institute of Medical Research; and CP Ventures Limited of Melbourne.

By 1990, Pac Bio intends to have expanded its scientific team to about 50 scientists. In addition to Pac Bio's own team, the company's scientific skill base is complemented by close interaction with scientific and medical researchers in the Garvan Institute of Medical Research and collaboration with a range of academic research institutions.

The Chairman of Pac Bio, Professor John Shine, is a leading figure in molecular biology. In 1987 he returned to Australia to join the Garvan as Deputy Director, and to take up the Chair of Molecular Biology at the University of New South Wales.

The principal focus of Pac Bio is to develop new and highly advanced cost-effective products specifically designed for the treatment and management of diseases of aging–products which will address multi-million dollar world markets in the 1990's. Research at Pac Bio is focusing on hormones, growth factors, cancer therapies and the cardiovascular and inflammatory areas.

PRODUCTS

Through a combination of its own research and licensing, Pac Bio is developing innovative and potentially major therapeutic biopharmaceuticals in the Australian and Asian market regions. It will also build a marketing and manufacturing base for an international, fully integrated biopharmaceutical company. Products under development include:

Human Growth Hormone

Pac Bio holds a worldwide license to commercialize biosynthetic human growth hormone (hGH) from mammalian cells and is evaluating with Cal Bio the nasal delivery of growth hormone using Cal Bio's proprietary NAZDEL system.

The human growth hormone is the first human pharmaceutical developed by recombinant DNA technology in Australia. The result of a series of unique technological developments, it is of major importance to the Australian biotechnology industry.

Lung Surfactant

The absence of adequate levels of surfactant, which frequently occurs in premature babies, causes the air sacs of the lung to collapse. Cal Bio has cloned genes for the protein components of lung surfactant essential for proper respiratory functions.

Pac Bio intends to conduct trials on this product which promises to help reduce infant mortality and enormous medical costs, and has licensed the product for Australasia and most of the Asian/Pacific region.

Nasal Drug Delivery System

Most current biotech therapeutic agents are proteins administered only by injection.

The NAZDEL technology has already been successfully applied to the nasal delivery of insulin in which Eli Lilly, Cal Bio's partner in this project, will pursue through to market launch. Cal Bio will make this technology available to Pac Bio.

For more information contact **Brian McNamee**, Managing Director, Darlinghurs, NSW.

ABC WELCOMES ADDITIONAL NEW MEMBERS FOR 1988

Agouron Pharmaceuticals, Inc.
La Jolla, California

Alfred Benzon, Inc.
Philadelphia, Pennsylvania

Consulting Statisticians, Inc.
Wellesley, Massachusetts

Enterovax Limited
Adelaide S.A.
Australia

Fujirebio America Inc.
Fairfield, New Jersey

HOM Consultancy
The Hague
The Netherlands

International Bio-Research (IBR)
Walsrode
Federal Republic of Germany

Lehigh University
Bethlehem, Pennsylvania

Michigan Biotechnology Institute
Lansing, Michigan

National Bureau of Standards
Boulder, Colorado

Northern Illinois University
DeKalb, Illinois

Ortho Biotech Imaging Products
Washinigton Crossing, New Jersey

Qlone Limited
Sherwood QLD.
Australia

Transia
Lyon
France

University of Illinois
Urbana, Illinois

Utah State University
Logan, Utah

Total current ABC membership: 178, representing 13 countries and 24 states.

Copyright ©1988 By: Association of Biotechnology Companies

DETAILS
Association of Biotechnology Companies
1120 Vermont Avenue, N.W.
Suite 601
Washington, D.C. 20005

Mr. SCHEUER. Thank you very much, Dr. Mackler.

Now, Mr. Godown, the last of our witnesses this morning, thank you for your patience. Take such time as you may need.

STATEMENT OF RICHARD D. GODOWN, PRESIDENT, INDUSTRIAL BIOTECHNOLOGY ASSOCIATION

Mr. GODOWN. Mr. Chairman, thank you very much for your patience, and I want to commend you and commend your staff for having recognized early on the contributions that biotechnology has to offer, and for being and representing a strong supporter on Capitol Hill. I would note for the record that your remarks we found very, very pleasing the other day at the Congressional Institute for the Future meeting on Tuesday, and we certainly welcome your strong support and your recognition.

I think I will take you up on your offer or invitation to comment on what has gone before today. It is kind of fun to go last. You get a chance to sit there and make some notes. I also have some prepared stuff that I want to get into the record, but first let me just comment on a number of points.

I would like to publicly applaud the House action last night in passing the trade bill, which contains within it that most especially important element for biotechnology in particular, and that is the process patent legislation that we are interested in. It is a fact that currently, without this change in the law, U.S. process patents have no extraterritorial effect, and so literally an invention which is patented here can be stolen, can be pirated offshore and manufactured, and that product can be brought back to our own shores and sold alongside your own patented product, side-by-side on the shelf, and you don't get a penny of royalty.

Mr. SCHEUER. That is totally unacceptable, totally unacceptable.

Mr. GODOWN. Exactly, exactly, and this legislation will correct that, and we want to commend that.

Also I would like to pick a little fight with a number of representatives of the administration who have testified here this morning. Commerce came, it seems to me, and they rained on your proposal, and I feel that they should not have. The Chiles-Kennedy bill, S. 1966, passed the Senate by a vote of 88 to 1. If indeed——

Mr. SCHEUER. And it passed last year. No, it was introduced last year and it passed in June, just a month ago.

Mr. GODOWN. Yes.

Mr. SCHEUER. Why in the world, if there were some constitutional questions there, didn't the Justice Department come up in timely fashion, before it was passed in the Senate and more than a few hours before we held this hearing, perhaps even a few days, perhaps with a little consultation and information sharing? For the life of me, I can't see why the OMB played what in all charity really seems to have been a mischievous role.

Mr. GODOWN. Dog in the manger.

Mr. SCHEUER. Yes, indeed.

Mr. GODOWN. If I may make so bold as to associate myself with your remarks, great minds think alike. [Laughter.]

I was about to say exactly that, and to add a comment not only on the question of constitutionality, if indeed there is a question on constitutionality—and that is a very, very nice argument to bring in at any time, and particularly at the last moment. One can always challenge a piece of legislation on the basis of whether or not it is constitutional. It seems to me the job of Congress is to enact. If there is a constitutional question, that is for the courts to decide.

Mr. SCHEUER. Well, it is also the job of Congress to consider constitutionality, and it seems to me it is the role of the Attorney General and the Justice Department, if there is a piece of legislation that has been considered over a several-year time frame and they feel that there is a constitutional question, for goodness sake, share that with us. Let's sit down and reason together, and let's work out the problem in a constructive, positive way, but not to throw this wrench into the machinery in the eleventh and a half hour, after it has long since passed the Senate and before we can even muster our resources to consider the constitutional question, during the House hearing.

Mr. GODOWN. Yes, sir, I agree with that. Let me walk out front just a little bit further and say that if indeed there is a question of conflict of interest because of the way that the board or the commission would be constituted, then it seems to me it was incumbent on those people raising the question to have raised it at an earlier time.

I would agree wholeheartedly with your remarks on the record earlier in this hearing today, that if indeed such a question exists or a problem exists, then a little jiggering by a couple of dedicated legal minds can certainly solve it. It has been solved in the past. The examples are manifest.

In any event, I found the position of Dr. Nelson of DOE particularly troublesome. He was suggesting that the leadership role as set forth in the legislation was perhaps not acceptable, and that there is already in existence a coordinating mechanism which is working quite well and, let alone, is going to work even better.

I would remind all of us, if I may, that an original version of this legislation was introduced in the Senate by Senator Domenici, I think, and in that legislation DOE was very directly placed in the leadership role. We took a poll, a survey of the members of the Industrial Biotechnology Association, and they unanimously rejected that as being a rational or reasonable way to approach it.

In our view, NIH should have a leading role because of the research that they have been involved in, where they have been, and what they are doing and what they are dedicated to. They are the obvious natural leader of the effort for mapping and sequencing the human genome, and given the size of the expenditures involved, I think it is terribly crucial that we get it done and we get it done right.

I wonder whether or not, since the Department of Commerce and also the Department of Energy have had some problems with the two bills which are in front of this panel for consideration, I wonder whether or not it is conceivable that we are looking at a question of jurisdiction or desirable jurisdiction or protecting your jurisdiction. The Office of Science and Technology Policy is, I think, an extremely useful bureaucratic instrument or an instrumentality of our current bureaucracy—and I don't use "bureaucracy" in a pejorative sense this time—but I do not think that it is——

Mr. SCHEUER. You are reserving your rights, I take it. [Laughter.]

Mr. GODOWN. Yes, but I do think that it is hardly the agency to carry out the job of coordination and oversight which is dictated here, nor indeed do I think that the circumstance which would pertain if no legislation is enacted—that is to say, that monies will continue to be devoted piecemeal to both DOE and NIH and a few other agencies in order to get mapping and sequencing of the human genome done in a piecemeal fashion—I don't think that is satisfactory, either.

Mr. SCHEUER. We will be hearing from Dr. Ruth Kirschstein pretty soon, but it seems to me that it is fairly obvious that—and I am not a scientist, and maybe this is a case of fools rush in where angels fear to tread—but it seems to me clear that both DOE and NIH have strengths, have obvious areas of involvement where they should be contributing, and it seems to me they ought to be equals and they ought to work together in good, easy, informal collaboration. There shouldn't be a leader-follower relationship there. They should function as colleagues in Government, all dedicated to the same goals, and they should work in informal, easy collaboration and coordination.

Mr. GODOWN. I would certainly like to associate myself with those remarks, Mr. Chairman, and say that both S. 1966 and H.R. 4502 represent superior means of accomplishing what currently is being done in a hodgepodge fashion.

Now to get on to just a couple of other points that I wanted to hit on, and then get some prepared materials into the record, on the question of whether or not we should—that is, in the U.S.—we should seriously think about the formation of consortia, Japanese-style, which have from the top down direction, or whether or not we should rather concentrate on what I will call cooperative research, I think is an essential question.

It is particularly true that the freestanding biotechnology companies—and that is a phrase that I use to distinguish them from the major pharmaceutical and chemical companies whose names you are aware of, who also do biotechnology—but the freestanding biotechnology companies are particularly concerned about the formation of consortia, because the way that they are doing business now is to find that niche that they can particularly serve through research and development, and then develop a product very fast and bring it to market.

They are concerned that a consortia operation might get in the way of this entrepreneurial development. I think we owe them the consideration of taking that into account as we formulate a national policy on how best to get where everybody wants to go, and would simply make the point that doing it through cooperative research rather than through a mandated consortia approach might be the better way.

Mr. SCHEUER. Well, you have certainly described the problem that has to be worked out to the satisfaction of the small firms, to liberate them to do their thing and to pick their niche and go for it.

Mr. GODOWN. Exactly. Let me make a point about either the National Biotechnology Policy Board or the National Biotechnology Policy Commission and about its membership. The membership dictated in S. 1966 would have the Government agencies—by name, NIH, NSF, USDA, Commerce, Defense, Energy, FDA, EPA, OSTP, and OMB—and then it mandates four people from the universities, four people from industry, one bioethicist, and one person from a philanthropic organization. We like that. That seems to us to be balanced.

Now I understand that one man's balance may be another person's tilt, but in your bill, sir, you do not set forth what the balance shall be, simply that there shall not be more Government members than there are members from other sectors of the country, and so——

Mr. SCHEUER. Excuse me. When you said philanthropic, did you sort of mean nonprofit? I don't know whether the Conservation Foundation is a philanthropic institution. It is surely a nonprofit. Did you mean an outfit like the Conservation Foundation, representative of somebody from the Conservation Foundation?

Mr. GODOWN. I think S. 1966 uses the word "philanthropic," but it also uses other words which would encompass, I think, other nonprofit organizations.

Mr. SCHEUER. Yes.

Mr. GODOWN. At any rate, in any event, let me finish off that point by saying that I think it is awfully important that the producers, the corporations who are involved in the research and the development of the product, those who are committed to bringing the products of this research and development to the marketplace, of necessity need to be the people who are consulted with on this committee in an appropriate fashion, so that regulations or policies which are going to have a direct impact on whether or not their products are ever going to see the light of day have at least that opportunity to be scrubbed over and to be considered by the people who are most directly concerned.

The companies are in fact down in the ditch with a shovel in their hands, shoveling away at the job of bringing the products to market. There are an awful lot of sidewalk superintendents, maybe a dime a dozen. We can get as many as we want. I think if you want to be a member of the team, come on down and grab a shovel. That is why in particular, I am using that analogy. I will testify that IBA prefers S. 1966 on this point to H.R. 4502, that is to say, the makeup of, in this case, the National Biotechnology Policy Board.

Let me now go to a discussion of the two bills. I will simply say that intense global competition has resulted in deliberate strategies by our competitors; that IBA believes it is time for the industrial, academic, and governmental communities to develop a cohesive and workable strategy for maintaining U.S. leadership in biotechnology, but I am not referring to an industrial policy where the Government tells the private sector what research to do or what goods to produce.

Rather, I am referring to creating a fairly nonbureaucratic way for Congress to systematically obtain expert advice on the issues that are central to the continued growth of the biotechnology industry, including these issues: the availability of private investment capital; Government support of basic research in the biological sciences; clear guidelines and communications by the regulatory agencies; the protection of intellectual property; and an international trade environment conducive to the export of biotechnology products.

H.R. 4502 and S. 1966 both address this need to develop a policy promoting biotechnology in the most appropriate way possible, namely by creating an expert National Biotechnology Policy Board or Commission, and while both bills provide for representation by three principal groups possessing expertise in these issues—namely the biotechnology industry, the academic research community, and Federal and State Government officials—IBA believes that S. 1966 is superior to H.R. 4502 in providing for a balanced representation of these groups. In particular, S. 1966 provides for substantially greater participation by both biotechnology industrial interests and academic/philanthropic biomedical research interests. We strongly recommend the Senate version of this title be adopted.

Mr. SCHEUER. Now at this point can I ask you, would you include in this consortium of interests to be represented, the public interest groups of the kind that Dr. Hollander represents?

Mr. GODOWN. I note that in the Senate bill there is provision for consultation with public interest groups, and I think that is an appropriate way for getting the interests of the various groups who direct themselves to a whole panoply of points which arise in the discussion of biotechnology. I think that that is perhaps the most efficient and effective and fair way to get that broad array of points of view on the record.

Mr. SCHEUER. But you wouldn't have them sitting in the mainstream with you and Government?

Mr. GODOWN. I think I would not.

Mr. SCHEUER. All right. Please proceed. Are you finished?

Mr. GODOWN. One more point on the human genome program: We recognize the importance of establishing a coordinated program to map and sequence the human genome and, based on the results of a survey of our members, we endorse the Human Genome Advisory Panel proposed. Knowing the entire human genomic sequence will allow scientists to more rapidly identify genes involved in human genetic diseases. More than 3,000 human genetic diseases have been defined but very few of the disease genes have been specifically identified.

Mapping and sequencing will enable us to better understand the genetic differences between individuals. Mapping and sequencing the genome will also help us to understand cancer cells better. Sequencing the genome could enable us to compare similar DNA sequences from humans and other animals to provide insight into evolutionary mechanisms.

Finally, it is possible that in the next 10 to 20 years, sufficient data will become available for the genome product to allow the three-dimensional shape of proteins to be predicted from their amino acid sequence. The ability to predict protein structure from the amino acid sequence will, in time, enable us to engineer proteins for therapeutic purposes more quickly, accurately, and functionally to treat human diseases.

We would propose that—I am sorry—let me say that while it is clear that sequencing the genome is likely to lead to significant public health and scientific benefits, many biologists believe that a crash program to sequence the entire human genome, as opposed to those genes which have been linked with disease states, may be wasteful and trivial—wasteful because within 5 years automated sequencing machines could be developed to reduce the cost of sequencing by more than 75 percent; trivial because as much as 95 percent of the DNA contained in the genome may be nonfunctional.

Finally I would say about the agricultural research section, which appears in the Senate bill but not in the House bill, agriculture is being revolutionized by biotechnology in terms of enhanced product quality, improved farm efficiency, reduced losses to pests and disease, and greater environmental acceptability. Despite its importance, however, the Federal Government has invested little in agricultural biotechnology.

IBA supports the promotion of U.S. capabilities in this area through expanding peer reviewed, competitive grant research programs in biotechnology. S. 1966 addresses this issue in two ways: It creates a major new research program in the specific area of biotechnology, and it creates an advisory panel to identify research priorities. We support both of these proposals.

Mr. Chairman, that does conclude my formal remarks.

[The prepared statement of Mr. Godown follows:]

IBA

Industrial Biotechnology Association

1625 K Street, N.W.
Suite 1100
Washington, D.C. 20006
(202) 857-0244
FAX: (202) 857-0237

TESTIMONY

OF

RICHARD D. GODOWN,

PRESIDENT,

INDUSTRIAL BIOTECHNOLOGY ASSOCIATION

ON H.R. 4502 AND S. 1966

BEFORE THE

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND THE ENVIRONMENT

AND THE

SUBCOMMITTEE ON SCIENCE, RESEARCH AND TECHNOLOGY

OF THE

HOUSE SCIENCE, SPACE AND TECHNOLOGY COMMITTEE

JULY 14, 1988

Directors

Chairman
George B. Rathmann
Amgen

Vice Chairman
Hugh A. D'Andrade
Schering Plough Corp.

Secretary
L. Patrick Gage
Hoffmann La Roche, Inc.

Treasurer
Jerry D. Caulder
Mycogen Corporation

Alberto E. Adam
American Cyanamid Co.

Will D. Carpenter
Monsanto Company

Ralph E. Christoffersen
The Upjohn Company

Nicholas M. Frey
Pioneer Hi Bred
International, Inc.

Ralph W. F. Hardy
BioTechnica International, Inc.

David A. Jackson
E.I. du Pont de Nemours & Co.

John R. Norell
Phillips Petroleum Company

Roger Salquist
Calgene, Inc.

Hubert J. P. Schoemaker
Centocor

Mark B. Skaletsky
Biogen Inc.

Robert A. Swanson
Genentech, Inc.

Mr. Chairmen and members of the subcommittees:

My name is Richard D. Godown. I am appearing before you today on behalf of the Industrial Biotechnology Association (IBA), a trade association of 84 companies that are using biotechnology to produce new healthcare, agricultural, and consumer products.

I would like to begin my testimony by commending Chairman Scheuer for his recognition of the contributions that biotechnology has made and will continue to make to the public health and the national economy. I should note that the Chairman and his staff were among our industry's earliest supporters on Capitol Hill, and that IBA very much appreciates his foresight and leadership in this area.

Biotechnology has produced new medical products to diagnose genetic and infectious diseases, such as cystic fibrosis and AIDS, as well as to treat cancer, prevent organ transplant rejection, treat diabetes and dwarfism and prevent the spread of hepatitis. Many others are currently being evaluated in clinical trials. Some agricultural biotechnology products to diagnose and treat animal diseases have already been marketed. In development are environmentally safe biological pesticides; plants resistant to drought, salt and other stress factors; genetically improved food animals; and a variety of other agricultural products.

International Competition in Biotechnology

In the United States, the biotechnology industry has traveled a traditional path, with research breakthroughs emanating from both the private and the public sectors and growth supported by a free enterprise system that encourages investment in new endeavors. Discoveries that first occurred in the research laboratories of healthcare companies, or in university and government laboratories and then transferred to industrial laboratories, have been developed and commercialized relatively quickly. This combination of publicly funded basic research and privately funded applied research and development resulted in the coming to fruition of the new industry.

The vast potential for biotechnology products has attracted worldwide attention. In 1986, revenues for U.S. biotechnology companies reached $650 million. In 1987, a major biotechnology product, tissue plasminogen activator, was approved and is available to treat the millions of people worldwide who have heart attacks. It will increase biotechnology sales significantly in 1988 and beyond. Worldwide sales figures for all biotechnology products are projected to be at $2.7 billion by 1990 and $40-75 billion by the year 2000.

By the mid-1980s, the immense promise of biotechnology had attracted the attention of governments around the world. A number of countries have now targeted biotechnology as a growth industry and established coordinated government/industry/university programs. For instance, in 1986, European governments spent an estimated $330 million to foster academic and industrial collaborations and to encourage scale-up of bioprocess technology. In the United Kingdom, the British Technology Group, a public corporation, was funded to assist in starting biotechnology companies. In West Germany, The Society for Biotechnological Research assists in technology transfer to industry. The Netherlands has a five-year plan to foster collaborations and bioprocessing scale-up. The Japanese government is coordinating private sector activities in biotechnology. And the biotechnology trade association in Japan, our most potent competitor in this area, expects biotechnology to account for 11 percent of that country's gross national product by the year 2000. The primary focus of these activities is to facilitate the transfer of technology from the university to industry and to speed the development of new products. The reason: To garner a share of the global market for biotechnology products.

In North America, this growth process essentially takes place through federal investment in basic scientific research and incentives to private industry, unlike the "top-down" approach that prevails in other countries, where government agencies generally implement industrial policies directly. The U.S. government concentrates on such areas as tax policy, research funding, technology education, domestic and international trade, patent law, and regulation of products and industrial practices to encourage development in the private sector. These policies are a critical element in the successful commercialization of any new technology, and, in their absence, development languishes.

Paradoxically, the essential strength of the U.S. system to encourage new industrial growth, i.e. its flexibility and lack of government-directed activities, is its major weakness as new markets become internationalized. Thus far, an informal interaction among the government, academe and industry has worked fairly well to identify issues and to propose courses of action. The result, we hope, will be a quickening in the rate of discovery and commercialization, leading to increased U.S. competitiveness in biotechnology.

However, informal interactions become insufficient when intense global competition has resulted in more deliberate strategies by our competitors. IBA believes that it is time for the industrial, academic, and governmental communities to develop a cohesive and workable strategy for maintaining U.S. leadership in biotechnology. I am not referring to an industrial policy where the government tells the private sector what research to do or what goods to produce. Rather, I am referring to creating a fairly nonbureaucratic way for Congress to systematically obtain expert advice on the issues that are central to the continued growth of the biotechnology industry, including:

- the availability of private investment capital;
- government support of basic research in the biological sciences;
- clear guidelines and communications by the regulatory agencies;
- the protection of intellectual property; and
- an international trade environment conducive to the export of biotechnology products.

H.R. 4502 and S. 1966 both address this need to develop a policy promoting biotechnology, in the most appropriate way possible, namely by creating an expert National Biotechnology Policy Board or Commission. While both bills provide for representation by the three principal groups possessing expertise on these issues, namely the biotechnology industry, the academic research community, and federal and state government officials, IBA believes that S. 1966 is superior to H.R. 4502 in providing for a balanced representation of these groups. In particular, S.1966 provides for substantially greater participation by both biotechnology industrial interests and academic/philanthropic biomedical research interests. IBA strongly recommends that the Senate version of this title be adopted.

Human Genome Program

S. 1966 also recognizes the importance of establishing a coordinated program to map and sequence the human genome. Based on the results of a survey of our members, IBA endorses the human genome advisory panel proposed in S. 1966.

There are a variety of reasons for seeking additional knowledge about the makeup of the human genome.

First, knowing the entire human genomic sequence will allow scientists to more rapidly identify the genes involved in human genetic diseases. More than 3,000 human genetic diseases have been defined, but very few of the disease genes have been specifically identified. Once these genes are identified, diagnostic tests and new treatments can be developed.

Second, mapping and sequencing the genome will enable us to better understand the genetic differences between individuals. Human beings differ from one another by approximately 1/10 of one percent of their nucleotides. These differences make virtually every human being distinct from every other human being, except for identical twins. These differences may have substantial medical implications when they are associated with systems that play important roles in protecting humans against disease. Particular differences in the genes of this system appear related with such autoimmune-related diseases as diabetes and multiple sclerosis.

Third, mapping and sequencing the human genome may also help us understand cancer cells better. Cancer cells differ from normal cells because they reproduce in an uncontrolled manner. One of the keys to understanding cancer is to determine the reasons underlying this difference. Studying the genome may enable us to determine how certain proteins function to cause cancer.

Fourth, sequencing the genome could enable us to compare similar DNA sequences from humans and other animals to provide insight into evolutionary mechanisms.

Finally, it is possible that in the next ten to twenty years, sufficient data will become available from the genome project to allow the three dimensional shape of proteins to be predicted from their amino acid sequence. The ability to predict protein structure from the amino acid sequence will in time enable us to engineer proteins for therapeutic purposes more quickly, accurately, and functionally to treat human diseases.

While it is clear that sequencing the genome is likely to lead to significant public health and scientific benefits, however, many biologists believe that a crash program to sequence the entire human genome, as opposed to those genes which have been linked with disease states, may be wasteful and trivial. Wasteful because within five years, automated sequencing machines could be developed to reduce the cost of sequencing by more than 75 percent. Trivial because as much as 95% of the DNA contained in the genome may be non-functional.

The success of sequencing the genome therefore depends heavily on advances in the relevant technologies. IBA proposes that the physical mapping of the human genome, which is immediately feasable and is considered a worthwhile endeavour by most biologists, be the first focus of the human genome initiative, with sequencing done primarily for sites associated with diseases until automated sequencing technology is developed to reduce the cost. Others have proposed a crash program to map and sequence the genome as quickly as possible. IBA believes that the Human Genome Advisory Panel established in S.1966 would provide an ideal forum for developing a consensus and a strategy for guiding this project in a cost effective manner.

Agricultural Research

Agriculture is being revolutionized by biotechnology, in terms of enhanced product quality, improved farm efficiency, reduced losses to pests and disease, and greater environmental acceptability. Despite its importance, however, the federal government has invested little in agricultural biotechnology. IBA supports the promotion of U.S. capabilities in this area through expanding peer-reviewed, competitive grant research programs in biotechnology.

S. 1966 addresses this issue in two ways. First, it creates a major new research program in a specific area of biotechnology. Second, it creates an advisory panel to identify research priorities. IBA supports both of these proposals.

Conclusion

Mr. Chairmen, IBA strongly supports S. 1966 and we urge you to do the same. Thank you for this opportunity to present our industry's views.

* * * *

Richard D. Godown joined IBA in December 1985. He spent three years with the government relations firm of Burson-Marsteller in Washington, D.C. and prior to that was general counsel of the National Association of Manufacturers and associate director of the Business Roundtable. Mr. Godown is a graduate of George Washington University Law School and a member of the District of Columbia Bar. He has become widely identified as a major spokesperson for the biotechnology industry, appearing frequently as a witness before Congressional Committees and speaking before various audiences and professional groups.

Mr. SCHEUER. Well, thank you very much, Mr. Godown. I agree with almost everything you have said. I have to say it is a little bit ironic to me that you want to exclude Ms. Hollander and her confreres in the public interest community from sitting at the table with you, when that is exactly the position that OMB takes in wishing to exclude private industry from sitting at the table with the various Government agencies involved.

Mr. GODOWN. I don't think there is an exclusion. I think very highly of Dr. Hollander and of her organization, and we look forward to working with them.

Mr. SCHEUER. Well, I know the Government agencies think very highly of you, too, but they don't want you in that circle. They are trying to exclude you from the loop, just as you are trying to exclude Dr. Hollander from the loop, and it seems to me that you belong in there at the table and so does Dr. Hollander. Am I being unfair?

Mr. GODOWN. No, no, no.

Mr. SCHEUER. The OMB perceives you just as you perceive Dr. Hollander, and I think they are both wrong.

Mr. GODOWN. Well, I think very highly of Dr. Hollander, so that I——

Mr. SCHEUER. No, this isn't personal. I am using her. She is representing the institution of public interest groups.

Mr. GODOWN. I think it is a legitimate question and inquiry, Mr. Chairman, if I may, on your part. Let me explain myself this way.

I think it is terribly important that in a national commission which is going to make recommendations and recommend policy for adoption by Congress and by the administration, that we have major elements of the burgeoning and developing biotechnology industry represented. It is essential that we have health care represented. That means that we should have somebody from recombinant DNA, and we also should have somebody who knows what they are talking about in the monoclonal antibody area. We certainly should have agriculture, as represented through the application of biotechnology to agriculture, and there are very, very important developments in the area of plant biotech and also animal biotech.

I know that there are only so many seats at the table. Now the question is——

Mr. SCHEUER. Well, the question is, is there one extra seat representing the public interest community that has played a very significant and positive role in moving the debate forward in this whole area of biotechnology—a very positive role, not a negative role or a carping role at all—is there a seat left for them?

Mr. GODOWN. Is that the only seat that is going to be requested? How many people are there, besides the organizations which we can now think of, who would come forward and say, "Ah, ha! Now they have a seat. We demand a seat."

Mr. SCHEUER. Well, how many seats should there be for industry? I don't know.

Mr. GODOWN. Four is fine, and four for academia.

Mr. SCHEUER. And the Government is amply represented. It seems to me there ought to be some representation for the public interest community, but all right. We have discussed that sufficiently at this point.

Dr. MACKLER. Can I——

Mr. SCHEUER. Do you wish to intervene, Dr. Hollander, at this point with a thought? Don't you want to belly up to the bar and participate?

Ms. HOLLANDER. Sure. I have already stated my position with respect to——

Mr. SCHEUER. No, no. I mean, don't you wish for the nonprofit community to be included in the loop, and not excluded and just asked a question once in a while?

Ms. HOLLANDER. Yes, I do, and I stated that in my testimony. I think as far as the need to get ample representation from all the communities, that the best way to do that—I agree with Dr. Godown's point that there are a lot of interests that need to be represented, and what I would like to see is a very diverse group at the top, which then——

Mr. SCHEUER. Excuse me, Dr. Hollander. I was wrong. We do have a roll call vote. It is on now. I have about 7 minutes to get over to the floor. We will continue with you first thing.

Have you finished, Dr. Godown? We will come back to you.

Mr. GODOWN. I would like to rejoin, yes.

Mr. SCHEUER. We will definitely come back to you, and then we will ask Dr. Kirschstein. In fact, Dr. Kirschstein can come up and join the table right now. We have reserved an empty place for her in a seat of honor.

[Recess taken.]

Mr. SCHEUER. Okay. I think we are rounding third base and headed toward home.

Why don't you finish, Dr. Godown, and then we will hear from Dr. Kirschstein, and then we will have some final questions.

Mr. GODOWN. Mr. Scheuer, thank you. Maybe for the record I ought to correct it. Although I love the encomium "Dr." Godown, my L.L.B. doesn't entitle me to it. Just plain "Counselor" will be fine.

Mr. SCHEUER. Well, we are talking globally today, and almost anywhere in the world an L.L.B. entitles you to be referred to as "Herr Doktor." Very well.

Mr. GODOWN. Sir, may I make a final point very quickly, and that is that in the interim I have had the opportunity to examine S. 1966, and I find that in title 2 where it sets forth the descriptions where the representatives are supposed to come from, it says "one individual representing national foundations, medical institutes or other philanthropic organizations." I would suggest that Anne Hollander's organization would qualify under "national foundations," and therefore I rest my case.

Mr. SCHEUER. I hate to be driven to make a choice here between an outfit like the Conservation Foundation and the Howard Hughes Medical Institute that has a lot of funding to contribute. Funding is important, but representing diverse points of view is also important. How would you cut it? Would you welcome in the Conservation Foundation and tell the Howard Hughes foundation that we would welcome their funding but we have no place for them at the table?

Mr. Godown. No, and with absolutely no intention to be facetious, this was the point that I was trying to get to before, that there are a goodly number of organizations who can signify a major interest in the workings of biotechnology or the products or the effects of biotechnology. Therefore, instead of attempting to construct a table which is big enough to include them all, I thought that S. 1966 handled it very nicely by calling for consultation with public interest groups.

I would simply suggest that as far as we are concerned, that is a desirable way of handling the question, but if Ms. Hollander showed up at the table as a national foundation, I would be delighted.

Mr. Scheuer. Good. You are holding the hand out. You are open-minded. Okay. Does that complete your testimony?

Mr. Godown. Yes, sir, and thank you.

Mr. Scheuer. Okay, Dr. Kirschstein. You have heard the Federal role questioned, criticized. I hate to put the burden on you of answering for all Federal agencies, but you are the lone survivor here of an endangered species, namely the Federal presence, so why don't you chat with us and answer what you wish to answer and deflect what you wish to deflect and give us your views?

Dr. Kirschstein. Mr. Scheuer, I wouldn't presume, nor will I, to speak for the other agencies.

Mr. Scheuer. Would you tip your mike down just a bit?

Dr. Kirschstein. Yes. I would say that in terms of NIH, it has been obvious for a long time and we have always provided for the obtaining of as much advice as possible from the broadest group of people. Indeed, the Congress in its wisdom, when it set up each of the various institutes of the National Institutes of Health, proposed and enacted into law that each of those institutes should have a National Advisory Council, and declared that two-thirds of the membership of that council should be scientific and one-third should be from members of the lay public knowledgeable in and interested in the particular aspects of the mission of that institute.

In the case of my own institute, the National Institute of General Medical Sciences, which is a basic science and research training institute, that one-third would consist of educators, individuals from industrial concerns, individuals from a number of organizations, of which Ms. Hollander's organization would be—not for our particular thing, because you are not involved in biomedical research—but something of the sort. Indeed, that has worked out extremely well. Those public members are very valued members to us on those advisory councils.

When the Recombinant DNA Advisory Committee was first set up at NIH—and it is the prototype for all of the advice in the guidelines for the new biotechnology industry—all of the groups were participatory and represented, and this has worked out extremely well, so I do not think that our department and NIH in particular would suggest that these people would not be represented. Indeed, we would welcome industrial representation, and should.

Mr. Scheuer. And public interest——

Dr. Kirschstein. And public interest groups. I just finished saying that. Absolutely.

Furthermore, since a membership has to be of a particular size, the advisory group would undoubtedly meet in public, and any public interest group or industrial representative or anyone else who, because he or she could not join the group, would come and provide testimony and interact with the advisory group. This is the way we run all our advisory committees.

Mr. **Scheuer**. All right. Now would you address yourself to the question of data collection in forms that are comparable?

We have a situation in the health care community, I am sure you are familiar with it. We can't compare hospitals in their operating expenses. We don't have comparable data on outcomes. We don't know what works and what doesn't work. We have rates of surgery, in terms of hysterectomies, tonsillectomies, appendectomies, that vary wildly from region to region and from coast to coast and internationally too.

Part of the reason that these extraordinary variations exist is, we aren't comparing apples to apples. We are comparing apples to oranges and grapefruit. The inability to achieve a common data base and common definitions is really grossly crippling our ability to be cost-effective, to eliminate waste and duplication and overlapping and all those things we have heard about for years. It really cripples our ability to be rational and to analyze effectively.

What do you think about the urgent need that you have heard expressed for the development of comparable data and comparable definitions and so forth?

Dr. **Kirschstein**. First of all, Mr. Scheuer, I understand what you are talking about completely. I am a physician, so I know what you are talking about in terms of the health care situation.

What Dr. Mackler addressed is at least partially correct. My own testimony talked about the fact that the data that are being assembled and the data bases do diverge considerably, and it is Dr. Lindberg's expression—the Director of the National Library of Medicine—that this is a data base Tower of Babel. He believes, and we do too, that the role of the National Library of Medicine, with the National Biotechnology Information Center, is to work together with all the Federal agencies to allow this to occur properly.

When you saw me reacting particularly to what Dr. Mackler was saying, it was specifically in regard to GenBank, because the data that are entered into GenBank, the nucleic acid sequence data, we think are well available to all the scientists and members of the industry who need them. What has happened is that until very recently the amount of material that has to be entered into GenBank and its European counterpart and now its Japanese counterpart, and all three are working together, is that it has been coming about and developing so rapidly that the data banks have not been able to keep up with it, with the way we have been able to provide them with funds.

Congress in its wisdom last year provided GenBank with $4 million. That was something in the order of six times as much money as it had had in any previous year, and as a result we have been able to begin to bring the backlog well under control—within another 6 months it will be under control—and to work out a system of a relational data base, which is one that will allow simple and easily accessible retrieval of information or anybody who wishes to use it.

This is being done in coordination with the people in Germany, at Heidelburg, the European Molecular Biology Laboratory, and with the Japanese group. My staff person who is in charge of the GenBank was in Heidelburg last week. The European people will be here in 6 months, and we talk on the telephone constantly, so I think it is evolving. We must remember that these data bases are coming—the data that we are putting into these data bases is just accumulating at a speed that none of us thought was feasible some time ago, and so it is an evolutionary process but we think it is working very well now.

Mr. SCHEUER. Dr. Hardy, one of the provisions of the Senate bill deals with research in so-called nontraditional applications of agriculture, nonfood, nonfiber, such as the biodegradable plastic bags derived from corn polymers. The bill calls for a Federal investment of about $75 million for each of the next 20 years. Do you think that a major part of the future of U.S. agriculture lies in the area of nontraditional uses for crop plants, that is, nonfood and nonfiber?

Dr. HARDY. Yes. Let me respond that I testified to a House committee last December that addressed that issue, and at that time went on record that I felt we needed to create a national commission to focus on developing a plan for research in these nontraditional uses of crops. We can produce more than the rest of the world needs or is willing to buy in the long term. There will be variations when droughts and events like that come along, but certainly the long-term trend is that the U.S. ability to produce agricultural products will far exceed the rest of the world's needs for them.

Clearly, then, to give our farmers other options, an area where we truly have an advantage over the Japanese—the Japanese do not have a Corn Belt, for example, they don't have the climate that we have—then I think it behooves us to provide a base of science, a base of technology that can enable us to do a number of other things beyond what we now can with agricultural products.

I am optimistic that if we focused in that area and focused on improving solar energy conversion, which is less than 1 percent at the moment, and moved that to 5 percent, if we focused on changing the composition of our traditional crops, if we focused on processing those, that even liquid fuels could be economically competitive, and that has a lot of side benefits to it. When you think about that, part of our carbon dioxide problem is in fact burning fossil fuels that were accumulated in the past. If we could more closely couple the use of carbon dioxide to produce crops and then their use as liquid fuels, and short-cycle that, then the greenhouse effect certainly would be less of a continuing problem than it is at this stage.

There are tremendous opportunities there. It is going to take a long-term commitment. It is going to take at least 10 years to do the type of science that we are talking about, to lay the base. We are juveniles in that area. There is essentially no research, as far as I am concerned, that is of much significance at this stage in terms of creating major additional uses. Yes, there are small things being done, like kanaf for paper and a few other things like that, but those are really modest uses compared to I think the major opportunities that we need to focus on, so I think it is——

Mr. SCHEUER. Major opportunities for nonfood, nonfiber——

Mr. HARDY. Nonfood, nontraditional uses of agriculture as they exist at this stage.

Mr. SCHEUER. Do you agree that the——

Dr. HARDY. This is where, in my judgment, if we added another $500 million a year in competitive grants, in the neighborhood of 40 percent of that money should be directed specifically to new uses for agricultural products.

Mr. SCHEUER. That is nontraditional?

Dr. HARDY. Nontraditional, yes.

Mr. SCHEUER. So you are talking about $200 million there. Now do you suggest we spend the $75 million a year, or should that be tripled?

Dr. HARDY. At that time I testified and supported the Harken bill, which I think is the basis of the $75 million, and certainly, yes, I think that is appropriate. I think it is something that we need to step-wise move into. We can't——

Mr. SCHEUER. Well, you just told us it ought to be $200 million, didn't you? Forty percent of $500 million.

Dr. HARDY. I said it should be 40 percent of $500 million or $200 million, stepped into over a period of 5 years.

Mr. SCHEUER. Very good.

Dr. HARDY. We are going from very little research at the moment, so I would think zero to $75 million is too aggressive in the first year, but certainly by the end of the fifth year the $200 million.

Mr. SCHEUER. Very good, so you step it up from $75 million to roughly $200 million over 5 years. Now if that is a proper level of funding for nontraditional agriculture, how would you fund continued research for traditional agriculture, food and fibers?

Dr. HARDY. Two ways. We have a marvelous——

Mr. SCHEUER. And at what order of magnitude or what level?

Dr. HARDY. We have ongoing research that is within the USDA, the Agricultural Research Service, the competitive States Research Service. We have major investments by the States that go into agricultural research. Most of those initiatives are ongoing research that produced modest but not dramatic changes, increases in the production system. I would leave those in place.

I would, in addition then, fund this activity that we are talking about for nontraditional uses. I would also fund some new initiative research in the traditional area, to enable us to significantly improve productivity in agriculture, to enable us to give higher value in use of foods and feeds. I am talking about leaner meats that would have greater healthfulness. I am talking about fruits that may have longer shelf life. I am talking about fruits that would have improved flavors, all these sorts of things that will have consumer appeal and give added value to the producer, and certainly be more desirable to the consumer.

The other area that I think we need to look at in agriculture is the environmental area, and clearly we need to move agriculture, if we can, away from a fertilizer- and pesticide-rich use activity to significantly lowering these. Biotechnology and biobased technologies provide that opportunity. We can think of in the longer term self-nitrogen fertilizing crops as alternates to nitrogen fertilizer. We can think of, I think over the next decade, much-expanded use of biologicals as biopesticides, as opposed to synthetic chemical pesticides. These in general will be more environmentally neutral.

Mr. SCHEUER. When you say "biological" you mean benign pesticides?

Dr. HARDY. Benign pesticides is another appropriate designation for them, in the most part. They are not all going to be benign, but in general they are going to be more benign than synthetic pesticides because they have been out in the environment over years and the environment has developed capabilities of degrading them, which is not the case for several of our synthetic chemical entitles.

Mr. SCHEUER. I take it that is welcome testimony from your point of view, Dr. Hollander?

Ms. HOLLANDER. Yes.

Mr. SCHEUER. All right. Now let me ask a question of Dr. Hardy, and perhaps Dr. Kirschstein too.

In the Senate bill, the National Center for Biotechnology Information at the National Library of Medicine is the central repository for genetic information on "processes that control health and disease." In your view, should genetic information on all organisms be stored there, or would it be useful to involve the National Agriculture Library as a repository of information on plant genetic data? Either of you?

Dr. KIRSCHSTEIN. I would say that I think it would be useful to have the Agriculture Department have that data, but have it accessed through a computer network through the National Library of Medicine——

Mr. SCHEUER. In a data-compatible——

Dr. KIRSCHSTEIN [continuing]. Centers, so that individuals who are interested in comparative data between plants, insects, yeast, the mouse, humans, could have easy access to the data right across the line through this computer network.

Dr. HARDY. I would agree that certainly there has to be one centralized area. There may be multiple sites that are coupled into this. As I mentioned in genome sequencing, I think one of the richnesses that will come out of genome sequencing will not be just the human genome itself, but will in fact be the comparisons between human genomes, animal genomes, plant genomes, and maybe insect and other genomes.

Mr. SCHEUER. Thank you.

The OTA report suggests that the basic research tax credit, which encourages companies to increase spending on basic research at universities and other nonprofit research institutions, be made a permanent part of the U.S. Tax Code. I suppose this question is for you, Mr. Godown. Do you think this will stimulate private sector investment in basic research, or perhaps is there a more efficient way to encourage industry support of research?

Mr. GODOWN. I think the answer is yes to the first part of your question. I think it is an elegant suggestion that the R&D tax credit be made a permanent part of the Tax Code, so that it doesn't go up and down and appear and disappear. It has indeed proved an incentive and has been important for the development of young biotechnology companies. We would very much welcome seeing its reinstitution and we are working towards that end.

Mr. SCHEUER. All right. Do Dr. Kirschstein or Dr. Hollander have any final thoughts before we close this hearing?

Ms. HOLLANDER. I have one that I would like to add, going back to the representation issue, which we have covered pretty well but——

Mr. SCHEUER. Which issue?

Ms. HOLLANDER. About the representation issue on the commission.

Mr. SCHEUER. Right, right.

Ms. HOLLANDER. We have covered that pretty well. I don't want to spend a lot of time on it, but I do have to differ with Mr. Godown's feeling that the Senate bill would encourage public interest representation. I think the way it is worded heavily implies that there would be more—that that person would be from a scientific foundation and not from a public interest group.

The Conservation Foundation in some senses straddles those communities, and so it is unfortunate that it has been the example we have been talking about. Other public interest groups, like the National Wildlife Federation or the Sierra Club or the Audubon Society, which might equally well represent those perspectives, don't seem to me to fall well or neatly into that category as cast in the Senate bill.

That's all I have to say.

Mr. SCHEUER. Anything more, doctor?

Dr. KIRSCHSTEIN. No, sir.

Mr. SCHEUER. Okay. Well, it is now 4:30. We have been at it exactly 7 hours, which I think is an all-time record for something, and the reason that we have been here so long is because these have been such extraordinarily interesting and intellectually stimulating panels on this subject, above all, that is intellectually stimulating in itself. We really have lost time with each successive panel.

This has been a marvelous panel. We are terribly grateful to all of you for staying in here and staying the course, as has been said. I can't think of who said that, but you have stayed the course and you have made a significant contribution to our thinking, for which we thank you. I am sure we will be in touch with you informally as we massage these two legislative proposals, and we thank you cordially for being with us at this very late hour.

The hearing is adjourned.

[Whereupon, at 4:30 p.m., the subcommittees adjourned, to reconvene at the call of the Chairs.]

○

89-952 (268)